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THE INFLUENCE OF THE DIMENSIONS OF IONS ON THE ELECTROMOTIVE FORCE OF A GALVANIC ELEMENT

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It is known that the electrode potentials of metals (in solutions of electrolytes) depend on the chemical nature of the electrolyte. In particular the electrode potentials of metals in solutions of KCl, KOH, and HCl of normal concentration have different values [1].

It is also known that the chloride ion has a stronger corrosive action on metals than the other halogen ions. Akimov [1] explains this by the fact that the chloride ion, because of its small dimensions, more easily penetrates the surface of the metal across the protective layer of oxides which cover it than do the other ions (the nitrate ion, sulfate ion, etc.).

Our experiments, conducted under conditions in which the possibility of formation of oxide layers on the metal was kept at a minimum, showed that a change in the electromotive force of a galvanic element and therefore of the electrode potential of the metal, which resulted when the chemical nature of the electrolyte was changed, depended on the magnitude of the ions which acted on the metal in solution.

EXPERIMENTAL

The galvanic element with which the experiments were carried out consisted of a zinc anode and a platinum cathode, dipping into a solution of electrolyte of the proper concentration. Both electrodes were prepared from platinum wire, which was sealed in a glass holder (sleeve); one of the electrodes was covered electrolytically with zinc (composition of bath: 150 g of $ZnSO_4$ and 100 g of water; current strength 50 ma.; time of plating 2 minutes) and then used as an anode. To reduce the oxide layer to a minimum, the electrodes were subjected to a simultaneous cathode treatment. They were placed in a bath with a 1 N solution of chemically pure sulfuric acid, joined to the negative pole of an accumulator battery (a third platinum electrode served as the positive pole) and an electric current passed through. The electrodes, thus treated with electrolytic hydrogen, were then washed with boiling water (twice distilled), dried with filter paper, and quickly transferred to the solution of electrolyte.

By means of a sensitive galvanometer, joined in series with a high resistance whose value could be varried from 1 to 100,000 ohms, and with the electrodes of the galvanic element, it was possible to measure the strength of the current flowing on the boundary of the element, and to calculate the electromotive force. The measurements were carried out under uniform conditions (temperature, total resistance of the hookup, etc.).

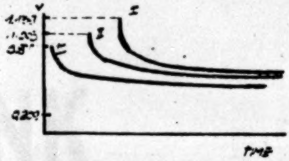
This method of measurement was worked out as the result of a large number of preliminary experiments carried out under other conditions. In particular preliminary experiments were carried out with the galvanic pairs: carbon-zinc, carbon-aluminum, carbon-iron, carbon-copper. "Coarser" measuring apparatus was employed, and the measurements were made with low resistances of the boundaries of the hookup.

Later on, in the tables, we shall employ several abbreviated symbols: $\underline{T}$ is the temperature of the electrolyte; $\underline{C}$ is the concentration of electrolyte; $\underline{C}_n$ is that of the normal, $\underline{C}_{sat.}$ that of the saturated solution; $\underline{V}_g$ is the e.m.f. of the galvanic element (in volts); R_o is the total resistance of the boundary of the circuit; $\underline{r}_a$ is the radius of the anion of the electrolyte; $\underline{r}_c$ is the radius of the cation of the electrolyte; $\underline{A}$ is the current strength on the boundary (in amperes).

RESULTS OF MEASUREMENTS

1. Data from Preliminary Experiments.

In Curves I, II, and III of the figure are shown the oscillograms from which it can be seen that the e.m.f. of the galvanic element changed depending on the chemical nature of the electrolyte (KCl, KBr, KI), and also on the duration. Despite the "coarse" method of measurement (galvanic pair of carbon and zinc, small total resistance of boundaries of the hookup, as a result of which polarization took place with great speed) it can be seen that the e.m.f. of the galvanic element changed as the chemical nature of the electrolyte changed. It was greatest (1.139 V) in a solution of KCl, less in a solution of KBr (1.003 V), and least of all (0.877 V) in a solution of KI.



Velocity of band 2 cm/sec. Temperature of solution 23°. Oscillograms: I - 2N KCl; II - 2N KBr; III - 2N KI.

As is known, the radii of the Cl, Br, and I ions vary [2,3,4]; according to Pauling, they have the values 1.81 A, 1.95 A, and 2.16 A, respectively. From this we may roughly draw the conclusion that with an increase in the radius of the anion (in the solution of electrolyte) the e.m.f. of the galvanic element has a tendency to decrease.

The experiments carried out by us with the same electrolytes (KCl, KBr, and KI) but with other galvanic pairs (C-Al, C-Cu, C-Fe) showed that a change in the e.m.f. of the galvanic element took place also when the other galvanic pairs were used. In all cases there was a tendency for the e.m.f. of the galvanic pair to decrease as the value of the anion radius increased. We were therefore forced to draw the conclusion that this influence was not specific, but was in accordance with some general law.

2. The Measurement of the E.M F. in Unsaturated Solutions

Later we investigated and eliminated the defects present in the preliminary experiments. To measure the e.m.f. we used more complete electrodes (platinum-platinum, zinc-plated); we increased the resistance of the boundaries of the galvanic element, introduced a treatment to reduce the electrodes with electrolytic hydrogen, etc. (as described in the section on method of measurement). As a result, we achieved reproducibility of results, and a decrease in the velocity of polarization of the electrodes.

Table 1 gives the data on measurements of the e.m.f in solutions of the

TABLE 1

Temperature of solutions 23°. Total resistance of hookup = 70,300 ohms. Galvanic pair: platinum-zinc.

NaCl					
C_n	3.17	2.11	1.58	1.05	0.78
V	1.052	1.074	1.063	1.071	1.074
KCl					
C_n	2.02	1.35	1.01	0.67	-
V	1.117	1.104	1.104	1.098	-
KBr					
C_n	2.03	1.35	1.01	0.67	-
V	1.027	1.027	1.014	1.014	-
KI					
C_n	1.95	1.30	0.97	0.65	-
V	0.842	0.862	0.851	0.842	-

alkali metals halides (the average values of 4 or 5 measurements are given).

As is shown by the numerical data of Table 1, the e.m.f. of the galvanic element fell as the anion radius increased and the cation radius of the electrolyte decreased ($r_{Na^{\cdot}} = 0.95$ A, $V_g = 1.07$; $r_c = 1.33$ A, $V_g = 1.117$).

3. The Measurement of the E.M.F. in Saturated Solutions

Table 2 lists the data on the measurements of the e.m.f. in saturated solustions of the alkali metal halides (average values of 5 to 7 measurements).

TABLE 2

Temperate of solutions 24°. Total resistance of hookup 70,300 ohms. Galvanic pair: platinum (saturated solution)-zinc.

Electrolyte	KCl	NaCl	KBr	KI	NaF
E.M.F.............	1.008	0.746	0.944	0.842	0.952

As can be seen from Table 2, the same rule holds true for saturated solutions: the e.m.f. of the galvanic element decreases as the radius of the anion increases and the radius of the cation in the electrolyte decreases:

$$V_g = \frac{\varkappa \cdot r_c}{r_a}$$

($\varkappa$ is a coefficient of proportionality)

EVALUATION OF RESULTS

1

We calculated the value of the coefficient of proportionality in the above equation for various electrolytes.

The radii of the ions, according to Pauling [2,3,4] equal:

$K^{\cdot}$	1.33 A	F'	1.36 A	Br'	1.95 A
$Na^{\cdot}$	0.95 A	Cl'	1.81 A	I'	2.16 A

Substituting the values of the ionic radii and the data of Table 2 in the equation, we obtain:

$$\underline{k}_{KCl} = \frac{1.81 \cdot 1.008}{1.33} = 1.371 \text{ V} \qquad \underline{k}_{NaCl} = \frac{1.81 \cdot 0.746}{0.95} = 1.421 \text{ V}$$

$$\underline{k}_{KBr} = \frac{1.95 \cdot 0.944}{1.33} = 1.383 \text{ V} \qquad \underline{k}_{NaF} = \frac{1.36 \cdot 0.952}{0.95} = 1.362 \text{ V}$$

$$\underline{k}_{KI} = \frac{2.16 \cdot 0.842}{1.33} = 1.367 \text{ V}$$

As can be seen from these calculations, the value of k for the five electrolytes given is almost constant. If we consider the fact that the concentrations of electrolytes in the saturated solutions differ considerably from each other [5]:

Electrolyte	Solubility at 25° (In moles/1000 g H_2O)
KCl	4.81
KBr	5.85
KI	8.86
NaCl	6.145
NaF	1.00

and the deviation from the average value does not exceed 3%, then we must conclude that the value of k for saturated solutions of electrolytes containing singly charged ions and the given galvanic pair is almost constant.

The average value of the coefficient k is 1.381 V. Starting with the constancy of the coefficient k, we made attempts to determine the "radii" of several univalent ions, in particular of $NH_4^\cdot$ and NO_3', by measuring the e.m.f. of the galvanic pair dipping into a saturated solution of NH_4Cl or KNO_3.

E.M.F. Pt (sat. solution NH_4Cl) Zn 1.0173 V,
E.M.F Pt (sat. solution KNO_3) Zn 0.8217 V.

Therefore:

$$\underline{r}_{NH_4^+} = \frac{1.81 \cdot 1.0173}{1.381} = 1.333 \text{ A},$$

$$\underline{r}_{NO_3'} = \frac{1.381 \cdot 1.33}{0.8217} = 2.23 \text{ A}.$$

Comparing the values of the radii of NO_3' and $NH_4^\cdot$ obtained in this manner with those calculated from the "covalent radius" we obtain fairly good agreement. See Table 3.

TABLE 3

Covalent radii [4]: H - 0.30 A; O - 0.74 A; N - 0.74 A

		$NH_4^\cdot$	NO_3'
Effective radius of the ion, calculated from ...	Covalent	0.74 + 0.3·2 = 1.34 A	0.74·3 = 2.22 A
	E.M.F	1.333 A	2.23 A

We may therefore draw the conclusion that by means of the measurement of the e.m.f. under definite conditions, by using the above equation, we can determine the "effective radius" of ions acting in solution on a metal.

2

Why does a change in the dimensions of the ions in a solution of an electrolyte produce an increase or decrease of the e.m.f.? No final answer to this question can yet be given. We can only suppose that the cause of the phenomenon of an electric current in a galvanic element is the action of the ions of the electrolyte on the surface of the metal in the solution. Apparently the anions of the electrolyte "bombard" the surface of the metal, as a result of which the "electron gas" of the metal undergoes constriction, and a kind of electron "pressure" penetrates the metal. The greater the number of anions acting on a unit surface of the metal at any time, the greater will be the "pressure on the electron gas". The increase in the e.m.f., related to the decrease in the radius of the anion of the electrolyte, indirectly confirms the latter supposition. In fact, the smaller the anion of the electrolyte, the greater the number of anions which can act simultaneously per unit of metallic surface submerged in the electrolyte, and the greater will be the constriction of the "electron gas" in the metal, and the greater the "pressure of the electron gas". On the other hand, apparently, "the constriction of the electron gas" is far from being uniform with different metals, and therefore the electrons will be transferred from a zone of high "electron gas pressure" to a zone of low pressure, i.e., they will pass along the conductor from one metal to the other (from the anode of the galvanic element to the cathode). The cations of the electrolyte must oppose the action of the anions on the metal as a result of their special action not only on the anions of the solution, but also on the "the electron gas" of the metal (in the case of exchange reactions), and hence the "retarding" action will appear all the stronger the smaller the value of the cation radius. The transfer of electrons from the metal (anode) leads to the positive ions of the metal breaking their mutual bonds, and being transferred, as a result, into the solution.

SUMMARY

1. The electromotive force of a galvanic element depends on the size (radius) of the ions present in a solution of electrolyte. It decreases as the radius of the anions increases and as the radius of the cations decreases.

2. The influence of the radius of the ions in a saturated solution of electrolyte on the e.m.f. can be expressed by the following empirical formula:

$$V_g \approx \frac{k \cdot r_c}{r_a},$$

where V_g is the e.m.f. of the galvanic element, k is the coefficient of proportionality, with almost constant value for univalent ions and a given galvanic pair; r_a is the radius of the anion, r_c is the radius of the cation.

3. The above empirical formula makes it possible to determine approximately the radius (effective) of singly charged ions in a solution.

4. In the light of these facts, we have expressed a hypothesis concerning the mechanism of the interaction of the ions of the electrolyte solution with the metal placed in solution.

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THE PHYSICO CHEMICAL ANALYSIS OF THE SYSTEMS: PYRIDINE-ETHYLANILINE AND QUINOLINE-ETHYLANILINE

I. INTERNAL FRICTION, SPECIFIC GRAVITY AND INDEX OF REFRACTION

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The question of the character of the relations between acids has drawn the attention of Hantzsch [1], Brönsted [1], N.S.Kurnakov and E.B.Shternin [2], M.I. Usanovich [3], and other investigators [4,5]. On the basis of their work, it has been determined that acids with different dissociation constants in many cases enter into chemical reactions with each other.

The formation of a chemical compound between two acids is easily explained by the modern theory of acids and bases [1]. From the point of view of this theory, this is a very natural phenomenon, and by analogy with the acids we have suggested a hypothesis concerning the presence of chemical reactions between two amines of different strength. This question, so far as we know, is not discussed in the literature, and has apparently not been the subject of special study. It was therefore of interest to investigate systems containing amines by the methods of physico-chemical analysis.

As a preliminary experimental investigation of this question, we carried out a physico-chemical analysis of the systems formed by ethylaniline with pyridine and quinoline with regard to internal friction, specific gravity, and index of refraction. We must note that these systems have not previously been investigated with regard to any of these properties.

We determined internal friction by means of an Ostwald viscosimeter of the covered type; specific gravity by means of a Regnault pycnometer with a narrow neck, and a capacity of about 8 ml, the specific gravity being determined with respect to water at 4°; the index of refraction was measured for the sodium line with a Pulfrich refractometer. The temperature was kept constant within a range of 0.05° by means of a suitable thermostat.

The Pyridine - Ethylaniline System

For the preparation of this system, we used pyridine which distilled completely at 115° at normal pressure: d_4^{20} 0.9820; n_D^{20} 1.5062.

After preliminary drying, the ethylaniline was fractionally distilled first at normal pressure, then in vacuum. For this work we took the fraction which boiled at 78.9-79° under a pressure of 8 to 9 mm of mercury: d_4^{20} 0.9623; n_D^{20} 1.5540

The internal friction and the specific gravity were determined at 0, 20, and

TABLE 1

Internal Friction of the Pyridine - Ethylaniline System

Expt. No.	C_5H_5N, mol. %	Internal friction (in centipoises)			Additive value of η at 0°	Deviation from additivity at 0°	$\alpha = \frac{\eta t_1 - \eta t_2}{t_2 - t_1}$	
		η	η	η			0° - 20°	20° - 70°
1	0	4.138	2.170	0.793	4.138	-	0.0984	0.0271
2	15	3.992	2.118	0.775	3.721	+ 0.271	0.0937	0.0269
3	25	3.820	2.030	0.750	3.443	+ 0.377	0.0895	0.0256
4	40	3.480	1.869	0.733	3.027	+ 0.453	0.0805	0.0227
5	50	3.214	1.742	0.705	2.749	+ 0.465	0.0736	0.0207
6	60	2.935	1.611	0.673	2.471	+ 0.464	0.0662	0.0188
7	75	2.421	1.379	0.610	2.055	+ 0.366	0.0520	0.0154
8	85	1.999	1.219	0.581	1.777	+ 0.222	0.0390	0.0128
9	100	1.360	0.968	0.508	1.360	-	0.0196	0.0092

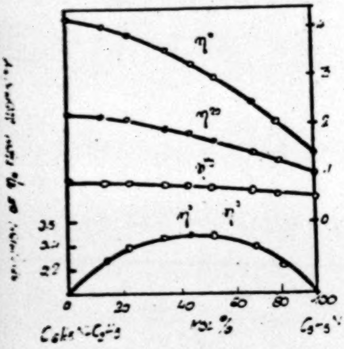

Fig. 1.

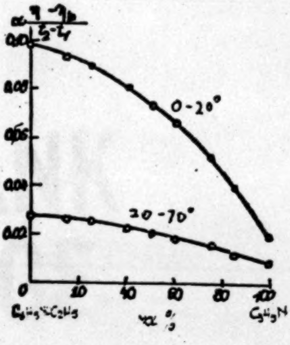

Fig. 2.

70°. In Table 1 and in Figs. 1 and 2 are listed the experimental data on internal friction, the deviation of this property at 0° from the additive value, and the temperature coefficients.

The results of the measurements of the specific gravity of the system are shown in Table 2 and Figs. 3 and 4.

The internal friction, as is known, is one of the properties most sensitive to changes in the molecular condition of the components when they are mixed together and the measurement of this property is a fairly accurate method of discovering a chemical compound [6] in liquid systems. In accordance with Dunstan's [7] classification, an isotherm of internal friction lying close to the additivity line corresponds to a normal system. A positive deviation from additivity or a maximum of the isotherms, is observed only in systems whose components react chemically with each other [5,8].

The isotherms of internal friction of the system pyridine - ethylaniline (Fig. 1) are curves convex to the axis of composition, and are characteristic for systems with chemical interaction of such a degree as to form compounds which are strongly dissociated in solution. The dissociation increases as the temperature rises, and this corresponds to the decrease in the convexity of the curves of

TABLE 2

Specific Gravity of the Pyridine – Ethylaniline System

Experiment No.	C_5H_5N, mol. %	C_6H_5N, vol. %	Specific gravity		
			d_4^0	d_4^{20}	d_4^{70}
1	0	0	0.9792	0.9621	0.9188
2	15	9.6	0.9817	0.9645	0.9204
3	25	17.6	0.9832	0.9657	0.9233
4	40	28.5	0.9870	0.9700	0.9251
5	50	38.3	0.9891	0.9718	0.9269
6	60	47.3	0.9914	0.9738	0.9282
7	75	65.7	0.9950	0.9772	0.9309
8	85	77.2	0.9973	0.9791	0.9320
9	100	100	1.0010	0.9825	0.9335

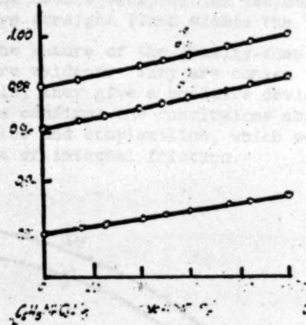

Fig. 3.

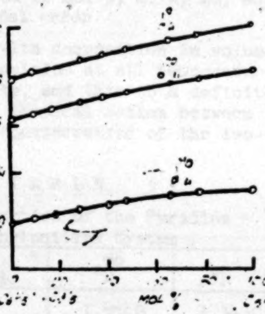

Fig. 4.

internal friction (Fig. 1). The deviation from additivity of viscosity at 0°, as can be seen from column 7 of Table 1 and from Fig. 2, has a maximum value for mixtures close to the composition of 50 mol.%, thus permitting us to judge the composition of the compound. In all probability, its composition corresponds to the formula: $C_6H_5NHC_2H_5 \cdot C_5H_5N$.

We calculated the absolute temperature coefficients of internal friction (α) between 0 and 20° and between 20 and 70° from the equation:

$$\alpha = \frac{t_1 - t_2}{t_2 - t_1}.$$

As can be seen from Fig. 2, the curves showing the relationship between the temperature coefficient of the system and composition are like the diagrams of internal friction; therefore they too characterize the pyridine – ethylaniline system as abnormal [6].

We investigated the specific gravity chiefly in order to calculate the internal friction. At the present time, despite a few exceptions, this property cannot be used as a characteristic for the investigation of binary liquid systems. E.V. Biron [9], on the basis of broad investigations, has determined that contraction of the system can result not only from chemical reaction, but from physico-mechanical processes as well. An increase in specific gravity can take place, for example, in case the molecules of the components differ in their dimensions and mixing permits them to be packed more densely. From this it follows that the isotherms of specific gravity can be convex to the axis of composition just as if there were a chemical reaction in the system, even though there is none. Therefore in the majority of cases it is impossible to determine the character of the behavior of the components in the system merely from the specific gravity curves. This must be regarded only as a foundation for other, more characteristic properties.

As V.Ya.Anosov has shown [10], the specific gravity of a normal system is additive when the composition is expressed in volume percent. Thus, the isotherms of this property must be more easily interpreted when the composition is expressed in volume percent.

Figs. 3 and 4 show the isotherms of specific gravity of the system pyridine – ethylaniline. The composition is expressed both in molecular percent (Fig. 3) and in volume percent (Fig. 4).

The density-composition isotherms, with composition in mol.%, at 0, 20, and 70° are straight lines within the limits of experimental error.

The nature of the density-composition isotherms, with composition in volume %, is more evident. They are convex to the axis of composition at all temperatures, that is, they give a positive deviation from additivity, and this to a definite degree confirms the conclusions about the presence of chemical action between pyridine and ethylaniline, which we had drawn from a consideration of the isotherms of internal friction.

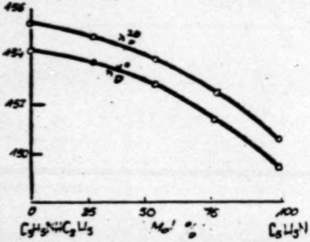

Fig. 5.

TABLE 3

Index of Refraction of the Pyridine – Ethylaniline System

C_5H_5N, mol. %	C_5H_5N, vol. %	n_D^{20}	n_D^{40}
0	0	1.5540	1.5430
25	17.6	1.5487	1.5380
50	38.3	1.5402	1.5290
75	65.7	1.5270	1.5153
100	100	1.5062	1.4951

Table 3 and Fig. 5 list the results of measurements of the system's index of refraction.

Numerous investigations have been conducted on refractometry of binary liquid systems by V.Ya.Anosov [11], who made the classification of isotherms of the index of refraction first given by A.Glazunov [12] more precise, broadened its meaning, and showed by means of considerable experimental data that refractometry could serve as one of the simplest methods of physico-chemical analysis.

It is clear from Fig. 5 that the isotherms of the index of refraction of the pyridine–ethylaniline system, measured by us at 20 and 40°, are curves which are very convex to the axis of composition.

This type of curve for the index of refraction, as has been found by one of the present authors and G.K.Aleksandrov [13], would correspond both to an abnormal system and to a system without chemical reaction which contained associated components.

In this case we must assume that the chemical reaction between pyridine and ethylaniline, observed in the curves of internal friction, is reflected also in the convexity of the isotherms of the index of refraction. This convexity is also maintained when the composition is expressed in terms of volume percent [14].

The Quinoline – Ethylaniline System

Quinoline was purified by fractional distillation, first at atmospheric pressure. Then the fraction boiling within the limits 236.6-236.9° was distilled in vacuum at 95°. In this work, we utilized the middle fraction, which was almost colorless: d_4^{20} 1.0933; n_D^{18} 1.6271.

The ethylaniline used was the same as in the system with pyridine.

Experimental data on internal friction and specific gravity are listed in Tables 4 and 5, and shown graphically in Figs. 6, 7, 8, and 9.

TABLE 4

Internal Friction of the Quinoline – Ethylaniline System

Expt. No.	C_9H_7N, mol. %	Internal friction (centipoises)			$\alpha = \frac{\eta_{t_1} - \eta_{t_2}}{t_2 - t_1}$	
		$\eta_{0°}$	$\eta_{20°}$	$\eta_{70°}$	0 - 20°	20 - 70°
1	0	4.138	2.170	0.793	0.0984	0.0275
2	15	5.342	2.647	0.852	0.1348	0.0359
3	25	6.139	3.025	0.906	0.1557	0.0424
4	35	7.011	3.451	0.956	0.1780	0.0499
5	50	8.415	3.854	1.147	0.2280	0.0542
6	60	9.053	4.025	1.219	0.2514	0.0562
7	65	9.150	4.083	1.285	0.2534	0.0560
8	70	9.155	4.102	1.298	0.2527	0.0561
9	75	9.091	4.067	1.329	0.2512	0.0548
10	85	8.455	4.051	1.315	0.2202	0.0547
11	100	7.290	3.885	1.293	0.1703	0.0518

TABLE 5

Specific Gravity of the Quinoline – Ethylaniline System

Expt. No.	C_9H_7N mol. %	C_9H_7N vol. %	Specific gravity		
			d_4^0	d_4^{20}	d_4^{70}
1	0	0	0.9792	0.9621	0.9188
2	15	13.3	0.9980	0.9818	0.9420
3	25	22.1	1.0090	0.9931	0.9544
4	35	31.8	1.0243	1.0097	0.9708
5	50	48.4	1.0449	1.0290	0.9904
6	60	56.5	1.0588	1.0447	1.0066
7	65	61.7	1.0652	1.0510	1.0137
8	70	66.9	1.0721	1.0569	1.0202
9	75	71.6	1.0774	1.0616	1.0291
10	85	83.1	1.0922	1.0770	1.0385
11	100	100	1.1093	1.0929	1.0549

The isotherms of internal friction of the quinoline - ethylaniline system (Fig. 6) are extremely significant and indicate a chemical reaction between the components.

A sharp maximum in the curve at 0° lies within the limits 30-35 mol.% of ethylaniline. This corresponds to the composition of a compound $C_6H_5NHC_2H_5 \cdot 2C_9H_7N$; as the temperature is raised, the maximum becomes more and more diffused as a result of the increase in thermal dissociation of the compound, and is slightly displaced in the direction of the more viscous quinoline. The curves for the temperature coefficient of internal friction of the quinoline - ethylaniline system, just as in the case of the preceding system, qualitatively repeat the course of the isotherm of internal friction and have a maximum corresponding to the same composition (Fig. 7).

Judging from the curves of internal friction, ethylaniline reacts chemically with quinoline much more strongly than with pyridine.

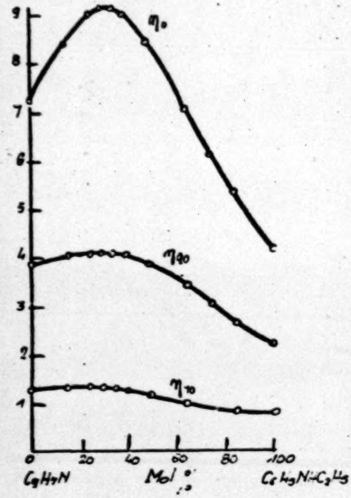

Fig. 6.

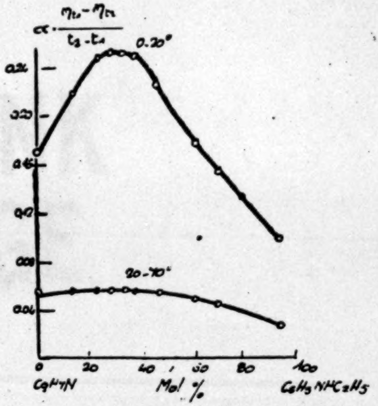

Fig. 7.

When the isotherms of specific gravity are plotted against composition expressed in molecular percent the curves are weakly convex to the axis of concentration (Fig. 8); they become more convex when the composition is expressed in volume percent (Fig. 9). Isotherms of this form for the specific gravity indicate the presence of compression in the system.

Table 6 and Fig. 10 give the results for the index of refraction measured by us at 20°.

The isotherms of the index of refraction (Fig. 10) are in the form of curves weakly convex toward the axis of concentration, when the latter is expressed in terms of molecular percent (we must note that the sign of the curvature is not changed when the change is made from molecular to volume percent). This form of curve for the index of refraction does not contradict our supposition that chemical

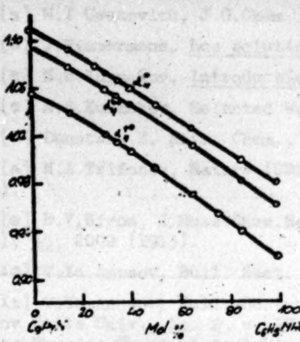

Fig. 8.

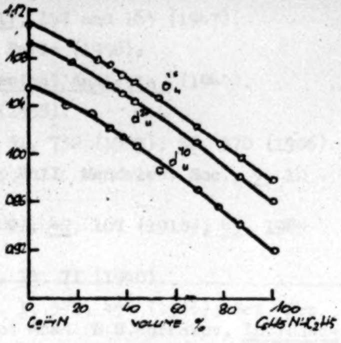

Fig. 9.

TABLE 6

Index of Refraction of the Quinoline – Ethylaniline System

C_9H_7N, mol.%	C_9H_7N, vol. %	n_D^{20}
0	0	1.5538
25	22.1	1.5736
50	48.4	1.5921
75	71.6	1.6086
100	100	1.6260

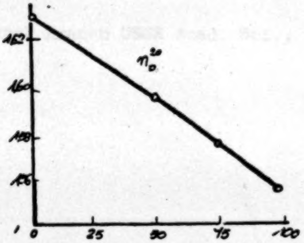

Fig. 10

reaction has taken place in the system.

Thus, chemical reaction between quinoline and ethylaniline, leading to a compound which is dissociated in solution into its components, is very clearly expressed in the isotherms of internal friction, and confirmed by the curves for specific gravity and index of refraction.

SUMMARY

1. Internal friction, specific gravity, and index of refraction have been investigated for the pyridine – ethylaniline system.

2. Internal friction, specific gravity, and index of refraction have been investigated for the quinoline – ethylaniline system.

3. The isotherms of internal friction, specific gravity, and index of refraction of both systems, as well as the curves for the temperature coefficient of internal friction show the formation of a chemical compound which undergoes dissociation in solution.

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THE HEAT CAPACITY OF LIQUIDS

III. THE HEAT CAPACITY OF HYDROCARBONS WITH SEVERAL UNCONDENSED NUCLEI

V. Ya. Kurbatov

We shall assume that the method of procedure is the same as in the preceding reports, except that in the case of diphenylmethane it was carried out in a thermostat chamber.

1. Diphenyl $(C_6H_5)_2$ 154.1; m.p. 70.8°, b.p. 254.98°.

θ	τ	C		θ	τ	C	
255.1	184.0	0.5648		154.3	98.2	0.4970	
255.3	184.0	0.5639	255.2	154.4	98.3	0.4943	154.4
255.2	183.9	0.5651	C = 0.5248	154.4	98.6	0.4921	C = 0.4940
255.3	184.1	0.5649	184.0	154.5	98.5	0.4937	98.4
255.1	183.9	0.5653		154.3	98.4	0.4929	
255.0	154.3	0.5520		128.6	98.3	0.4800	
255.1	154.5	0.5535	255.0	128.0	98.3	0.4791	128.1
254.9	154.4	0.5513	C = 0.5126	128.0	98.3	0.4782	C = 0.4805
254.9	154.5	0.5539	154.4	128.0	98.5	0.4827	98.4
255.1	154.3	0.5523		127.9	98.5	0.4827	
255.0	128.1	0.5422		184.2	128.5	0.5182	
255.1	128.0	0.5421	255.0	184.3	128.0	0.5131	184.0
255.0	128.0	0.5434	C = 0.5027	183.9	128.0	0.5155	C = 0.5162
255.0	127.9	0.5431	128.1	184.0	128.0	0.5144	128.1
254.9	128.2	0.5427		183.6	128.0	0.5198	
255.1	98.4	0.5319		154.1	128.0	0.5057	
255.0	98.6	0.5325	255.0	154.2	128.5	0.5061	154.4
255.0	98.5	0.5314	C = 0.5019	154.7	128.0	0.5012	C = 0.5049
255.1	98.3	0.5331	98.4	154.3	128.0	0.5064	128.1
254.9	98.3	0.5307		154.7	128.0	0.5051	
184.0	98.3	0.5023		184.2	154.1	0.5249	
184.1	98.5	0.5002	184.0	183.9	154.2	0.5232	184.0
183.9	98.2	0.5011	C = 0.5013	183.9	154.7	0.5278	C = 0.5251
183.9	98.4	0.5033	98.4	184.0	154.3	0.5262	154.4
184.1	98.6	0.4994		184.0	154.7	0.5234	

$$C_t = 0.3990 + 0.0007512\,\underline{t},$$
$$MC_t = 61.49 + 0.10576\,\underline{t}.$$

2. Diphenylmethane $C_6H_5CH_2C_6H_5$ 168.1; m.p. 26.5°; b.p. 262.8°.

θ	τ	$\underline{C}$		θ	τ	$\underline{C}$	
253.2	29.2	0.4824	$C_{29.2}^{253.3} = 0.4851$	128.1	29.1	0.4371	$C_{29.2}^{127.9} = 0.4389$
253.6	29.1	0.4879		127.9	29.2	0.4413	
253.1	29.3	0.4850		127.8	29.3	0.4383	
208.2	29.7	0.4702	$C_{29.5}^{208.2} = 0.4705$	99.7	29.4	0.4292	$C_{29.2}^{99.5} = 0.4272$
208.1	29.1	0.4711		99.5	29.0	0.4249	
208.4	29.6	0.4702		99.3	29.1	0.4275	
184.1	29.2	0.4598	$C_{29.3}^{184.1} = 0.4607$	79.2	29.1	0.4189	$C_{29.4}^{79.3} = 0.4192$
184.0	29.1	0.4608		79.1	29.6	0.4199	
184.2	29.6	0.4615		79.6	29.4	0.4197	
155.1	29.0	0.4504	$C_{29.1}^{155.2} = 0.4492$	54.5	26.7	0.4084	$C_{26.7}^{54.6} = 0.4086$
155.2	29.0	0.4472		54.9	27.3	0.4085	
155.3	29.2	0.4400		54.6	26.8	0.4089	

$$C_t = 0.3763 + 0.0007919\ \underline{t},$$
$$MC_t = 63.25 + 0.1337\ \underline{t}.$$

Comparison with data of Hofman, Parks, and Daniels

Hofman		Formula of V.Kurbatov
28.8°	0.379	0.396
39.1°	0.384	0.401

3. Diphenylethane: $C_6H_5CH_2CH_2C_6H_5$ 182.1; m.p. 52.8°; b.p. 284°.

θ	τ	$\underline{C}$		θ	τ	$\underline{C}$	
254.6	54.2	0.4959	$C_{54.2}^{254.3} = 0.4955$	154.4	54.2	0.4565	$C_{54.2}^{154.2} = 0.4575$
254.4	54.2	0.4952		154.3	54.2	0.4568	
254.1	54.2	0.4954		154.0	54.2	0.4569	
254.1	54.2	0.4955		154.1	54.2	0.4598	
217.1	54.2	0.4807	$C_{54.2}^{217.2} = 0.4811$	98.2	54.2	0.4366	$C_{54.2}^{98.3} = 0.4349$
217.1	54.2	0.4809		98.4	54.2	0.4366	
217.0	54.2	0.4816		98.3	54.2	0.4323	
216.6	54.2	0.4812		98.3	54.2	0.4341	
182.3	54.2	0.4692	$C_{54.2}^{182.1} = 0.4676$				
181.8	54.2	0.4676					
182.0	54.2	0.4641					
182.1	54.2	0.4685					

$$C_t = 0.3755 + 0.0007792\ \underline{t},$$
$$MC_t = 68.38 + 0.141814\ \underline{t}.$$

t	MC_t (formula)	MC_t (Smits, Andrew)
298.5	70.5	70.4
259.8	65.0	66.0

Formula for data of Smits: $MC_t = 67.2 + 0.142\ \underline{t}$.

4. Stilbene: $C_6H_5CH{=}CHC_6H_5$ 180.01; m.p. 124.2°; b.p. 307.8°.

Experimental data of V.Kurbatov

θ	τ	C		θ	τ	C	
304.9	134.8	0.5149	$C^{305.2}_{134.8} = 0.5149$	304.9	217.6	0.5472	$C^{305.2}_{217.4} = 0.5485$
304.8	134.8	0.5168		304.8	217.4	0.5468	
305.6	134.8	0.5133		305.6	217.5	0.5447	
305.5	134.8	0.5146		305.5	217.1	0.5433	
254.0	134.8	0.4981	$C^{254.3}_{134.8} = 0.4965$	254.0	217.6	0.5291	$C^{254.3}_{217.4} = 0.5279$
254.5	134.8	0.4937		254.5	217.4	0.5252	
254.4	134.8	0.4969		254.4	217.5	0.5276	
254.9	134.8	0.4969		254.3	217.1	0.5297	
217.6	134.8	0.4836	$C^{217.4}_{134.8} = 0.4837$	304.9	254.0	0.5531	$C^{305.2}_{254.3} = 0.5589$
217.4	134.8	0.4836		304.8	254.5	0.5599	
217.5	134.8	0.4838		305.6	254.4	0.5597	
217.1	134.8	0.4838		305.5	254.3	0.5540	

$$C_t = 0.3566 + 0.0007224\,\underline{t},$$
$$MC_t = 64.20 + 0.1300\,\underline{t}.$$

5. Tolane: $C_6H_5C{\equiv}CC_6H_5$ 178.08; m.p. 61°; b.p. 302°.

Experimental data of V.Kurbatov

θ	τ	C		θ	τ	C	
303.2	65.2	0.4911	$C^{303.5}_{65.2} = 0.4916$	255.1	117.3	0.4812	$C^{255.2}_{117.6} = 0.4830$
303.8	65.4	0.4919		255.0	117.9	0.4851	
303.7	65.0	0.4917		255.3	117.3	0.4830	
303.3	65.2	0.4917		255.4	117.9	0.4827	
255.1	65.1	0.4728	$C^{255.2}_{65.2} = 0.4728$	184.3	117.9	0.4542	$C^{184.2}_{117.6} = 0.4551$
255.0	65.0	0.4732		184.7	117.3	0.4563	
255.3	65.3	0.4730		184.0	117.3	0.4584	
255.4	65.4	0.4722		183.9	117.9	0.4515	
184.3	65.2	0.4446	$C^{184.2}_{65.2} = 0.4449$	303.2	255.1	0.5652	$C^{303.5}_{255.2} = 0.5660$
184.7	65.4	0.4447		303.8	255.4	0.5670	
184.0	65.0	0.4453		303.3	255.3	0.5689	
183.9	65.2	0.4450		303.7	255.0	0.5649	
117.3	65.4	0.4182	$C^{117.6}_{65.2} = 0.4188$	303.8	184.3	0.5249	$C^{303.5}_{184.2} = 0.5278$
117.9	65.1	0.4184		303.2	184.7	0.5298	
117.3	65.1	0.4181		303.7	184.0	0.5281	
117.9	65.2	0.4185		303.3	183.9	0.5284	
303.2	117.3	0.5103	$C^{303.5}_{117.6} = 0.5112$	255.1	184.3	0.5168	$C^{255.2}_{184.2} = 0.5191$
303.8	117.9	0.5123		255.0	184.7	0.5206	
303.7	117.3	0.5114		255.3	184.0	0.5193	
303.3	117.9	0.5108		255.4	183.9	0.5197	

$$C_t = 0.3468 + 0.0007844\,\underline{t},$$
$$MC_t = 61.77 + 0.1388\,\underline{t}.$$

6. Styrene: $C_6H_5CH{=}CH_2$ 104.6; m.p. 146.4°.

θ	τ	C		θ	τ	C	
139.2	21.0	0.4450	$C^{139.1}_{21.1} = 0.4453$	76.6	16.6	0.4182	$C^{76.4}_{16.7} = 0.4183$
138.8	21.3	0.4455		76.5	16.5	0.4186	
138.9	21.0	0.4449		76.4	16.9	0.4181	
139.5	21.1	0.4461		76.1	16.9	0.4183	

θ	τ	C		θ	τ	C	
109.1	20.1	0.4339	$C_{20.2}^{109.1} = 0.4341$	54.3	16.0	0.4102	$C_{16.1}^{54.2} = 0.4103$
109.3	20.3	0.4338		54.3	16.3	0.4106	
109.1	20.2	0.4346		54.1	16.1	0.4102	
109.3	20.2	0.4341		54.1	16.0	0.4102	
99.1	16.7	0.4282	$C_{16.8}^{99.3} = 0.4285$				
99.6	16.8	0.4287					
99.4	16.9	0.4289					
99.1	16.8	0.4282					

$$C_t = 0.3819 + 0.0007784\ \underline{t},$$
$$MC_t = 53.55 + 0.1090314\ \underline{t}.$$

7. Triphenylmethane: $(C_6H_5)_2CHC_6H_5$ 244.13; m.p. 92°; b.p. 359°.

θ	τ	C		θ	τ	C	
342.5	99.8	0.5490	$C_{99.8}^{342.2} = 0.5490$	199.8	99.8	0.5065	$C_{99.8}^{199.8} = 0.5055$
341.8	99.8	0.5436		200.1	99.9	0.5032	
342.1	99.8	0.5508		199.5	99.7	0.5056	
342.4	99.8	0.5526		199.2	99.8	0.5069	
303.4	99.8	0.5326	$C_{99.9}^{303.2} = 0.5337$	342.5	199.8	0.5899	$C_{199.8}^{342.2} = 0.5888$
301.8	99.9	0.5335		341.8	200.1	0.5875	
305.1	99.7	0.5321		342.1	199.5	0.5892	
305.2	99.8	0.5332		342.4	199.2	0.5886	
254.1	99.9	0.5170	$C_{99.9}^{254.2} = 0.5152$	303.4	199.8	0.5733	$C_{199.8}^{303.2} = 0.5758$
254.2	99.7	0.5155		301.8	200.1	0.5771	
254.2	99.9	0.5121		305.1	199.5	0.5752	
254.1	99.8	0.5160		305.2	199.2	0.5777	
199.8	99.4	0.4970	$C_{99.5}^{199.8} = 0.4959$	254.1	199.8	0.5542	$C_{199.8}^{254.2} = 0.5560$
200.1	99.5	0.4966		254.2	200.1	0.5551	
199.5	100.1	0.4947		254.2	199.5	0.5566	
199.2	100.2	0.4953		254.1	199.2	0.5581	
154.4	99.4	0.4629	$C_{99.8}^{154.3} = 0.4643$	342.5	254.1	0.6100	$C_{254.2}^{342.2} = 0.6104$
154.3	99.5	0.4662		341.8	254.2	0.6123	
154.2	100.1	0.4645		342.1	254.2	0.6109	
154.4	100.2	0.4642		342.4	254.1	0.6104	
342.5	99.9	0.5481	$C_{154.3}^{343.2} = 0.5472$	303.4	254.1	0.5961	$C_{254.2}^{303.2} = 0.5943$
341.8	99.7	0.5498		301.8	254.2	0.5933	
342.1	99.9	0.5495		305.1	254.2	0.5941	
342.4	99.8	0.5416		305.2	254.1	0.5933	
303.4	99.8	0.5378	$C_{99.8}^{303.2} = 0.5345$	342.5	303.4	0.6298	$C_{303.2}^{342.8} = 0.6292$
304.8	99.9	0.5301		341.8	301.8	0.6290	
305.1	99.7	0.5331		342.1	305.1	0.6288	
305.2	99.8	0.5369		342.4	305.2	0.6292	
254.1	99.8	0.5153	$C_{99.8}^{254.2} = 0.5124$				
254.2	99.9	0.5107					
254.2	99.7	0.5119					
254.1	99.8	0.5117					

$$C_t = 0.3730 + 0.00079644\ \underline{t},$$
$$MC_t = 89.05 + 0.1944\ t.$$

Comparing the formulas for molecular heat capacity, we obtain:

$C_6H_5C_6H_5$	$61.49 + 0.10576\ t$
$C_6H_5CH_2C_6H_5$	$63.25 + 0.1337\ t$
$C_6H_5CH_2CH_2C_6H_5$	$68.38 + 0.1398\ t$
$C_6H_5CH{=}CHC_6H_5$	$64.20 + 0.1300\ t$
$C_6H_5C{\equiv}CC_6H_5$	$61.77 + 0.1388\ t$
$(C_6H_5)_3CH_2$	$89.01 + 0.1944\ t$

Thus, a decrease of CH_2 in the molecule corresponds to:

$$\Delta MC_{CH_2} = \frac{5.2 + 1.7}{2} = 3.4;$$

A decrease of H_2:

$$\Delta MC_{H_2} = \frac{12.49 + 4.13}{2} = 8.41.$$

Substitutfng an H in $(C_6H_5)_2CH_2$ by C_6H_5 to get $(C_6H_5)_2CHC_6H_5$:

$$\Delta MC_{H \rightarrow C_6H_5} = 89.05 - 63.20 = 25.9$$

These values are less than those obtained in similar operations with more simply constructed compounds, i.e., without a large number of atoms, as will be shown further on. The transition from ethylbenzene to styrene: $41.9 - 39.8 = 2.1$ gives a value of the same order as in the cases of dibenzyl, stilbene, and tolane (cf. above).

The values of the listed temperature coefficients of heat capacity are compared in the following table:

	MC_0	$\frac{dMC}{dt}$	$\zeta = \left(\frac{dMC}{dt}\right) MC_0$
$C_6H_5CH_3$	35.7	0.085	0.0022
$C_6H_5CH_2CH_3$	41.9	0.099	0.0024
$C_6H_5CH{=}CH_2$	39.75	0.1034	0.0020
$C_6H_5C_6H_5$	61.49	0.1058	0.0017
$C_6H_5CH_2C_6H_5$	63.2	0.1337	0.0020
$C_6H_5CH_2CH_2C_6H_5$	68.38	0.1398	0.0020
$C_6H_5CH{=}CHC_6H_5$	64.20	0.1300	0.0020
$C_6H_5C{\equiv}CC_6H_5$	61.77	0.1388	0.0021
$(C_6H_5)_2CHC_6H_5$	89.1	0.1944	0.0021
			0.0021

Thus, the average coefficient of heat capacity found for hydrocarbons containing many phenyl groups is:

$$\zeta = \frac{dMC}{dt \cdot MC_0} = 0.0021$$

Average atomic heat capacity

	MC_0	ν	MC_0/ν
$(C_6H_5)_2$	61.5	22	2.7
$C_6H_5CH_2C_6H_5$ ...	63.2	25	2.5
$(C_6H_5CH_2)_2$	68.4	28	2.4
$C_6H_5CH{=}CHC_6H_5$..	60.8	26	2.3
$C_6H_5C{\equiv}CC_6H_5$ ...	61.8	24	2.6
$C_6H_5CH{=}CH_2$	39.8	16	2.5
$(C_6H_5)_3CH_2$	91.1	35	2.9
		Average	2.6

Thus, the average atomic heat capacity of hydrocarbons with several phenyl rings is almost the same as for benzene hydrocarbons.

The fact that the linear formulas correspond to the experimental data is confirmed by the following tables:

Diphenyl

θ	τ	Exptl.	Calcul.	θ	τ	Exptl.	Calcul.
255.2	184	0.5648	0.5642	184.0	128	0.5162	0.5162
255.2	154	0.5526	0.5497	154.0	128	0.5049	0.5051
255.0	128	0.5427	0.5428	184.0	98	0.5031	0.5094
255.0	98	0.5319	0.5317	154.0	98	0.4940	0.4920
184.0	154	0.5251	0.5259	128.0	98	0.4805	0.4839

Diphenylmethane

253.3	29.2	0.4851	0.4919
208.2	29.5	0.4705	0.4715
184.1	29.3	0.4605	0.4606
155.2	29.1	0.4492	0.4492
127.9	29.2	0.4389	0.4284
99.5	29.2	0.4272	0.4276
79.3	29.4	0.4192	0.4193
54.6	26.7	0.4089	0.4085

Tolane

303.5	255.1	0.5660	0.5660
303.5	184.2	0.5284	0.5278
255.2	184.2	0.5191	0.5192
303.5	117.6	0.4931	0.5107
255.2	117.6	0.4931	0.4830
303.2	65.2	0.4916	0.4911
255.4	65.4	0.4728	0.4723
184.2	117.6	0.4451	0.4548
184.2	65.2	0.4449	0.4374
117.6	65.2	0.4188	0.4186

Dibenzyl

254.3	54.2	0.4955	0.4960
217.2	54.2	0.4811	0.4809
182.1	54.2	0.4677	0.4674
154.2	54.2	0.4565	0.4565
98.3	54.2	0.4349	0.4349

Styrene

139.2	21.1	0.4453	0.4422
109.1	20.2	0.4341	0.4221
99.3	16.8	0.4285	0.4270
76.4	16.7	0.4183	0.4175
54.2	16.1	0.4103	0.4093

Stilbene

305.2	254.3	0.5589	0.5589
305.2	217.4	0.5485	0.5455
254.3	217.4	0.5279	0.5475
305.2	134.8	0.5159	0.5149
254.3	134.8	0.4965	0.4961
217.4	134.8	0.4837	0.4837

Triphenylmethane

342.8	303.2	0.6292	0.6292
342.8	254.2	0.6104	0.6104
303.2	254.2	0.5943	0.5952
342.2	199.8	0.5888	0.5888
303.2	199.8	0.5758	0.5733
254.2	199.8	0.5560	0.5537
342.2	99.8	0.5480	0.5489
303.2	99.8	0.5337	0.5330
254.2	99.9	0.5152	0.5139
199.8	99.5	0.4955	0.4920
154.3	99.3	0.4643	0.4641

SUMMARY

1. The heat capacities of liquid polyphenyl hydrocarbons and of styrene have been investigated at many intermediate temperatures.

2. In each case, the relationship to the temperature can be expressed by a linear formula.

3. An approximate rule is proposed for the composition of molecular heat heat capacity from the atomic values.

4. A law is proposed for the constancy of the reduced temperature coefficient of heat capacity (τ = 0.0021).

5. A law is proposed for the constancy of the average atomic heat capacity in this series of homologs.

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THE AMIDATION OF DIBASIC CARBOXYLIC ACIDS

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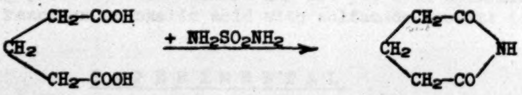
We have recently shown [1] that sulfamide reacts with monobasic carboxylic acids to form amides of the carboxylic acids according to the scheme:

$$RCOOH \xrightarrow{+\ NH_2SO_2NH_2} RCONH_2.$$

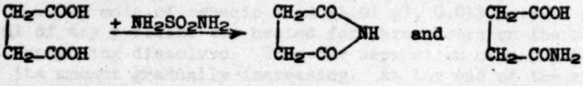
In this work we report on the results of experiments on the amidation of dibasic carboxylic acids with sulfamide in a solution of pyridine. The direction of the reaction of sulfamide with dibasic carboxylic acids depends on the type of acid. The complete amides are easily obtained in good yield only from dibasic acids with carboxyls far apart, beginning with adipic acid. Thus, for dibasic acids of this type, the reaction takes place in the same way as for monobasic acids, i.e., according to the scheme:

$$HOOC(CH_2)_4COOH \xrightarrow{+\ 2NH_2SO_2NH_2} NH_2CO(CH_2)_4CONH_2.$$

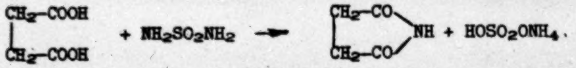
With dibasic acids which easily give internal anhydrides, such as glutaric and succinic acids, we did not succeed in obtaining the corresponding complete amides under any conditions. The action of a single mole of sulfamide on glutaric acid gave a good yield of glutarimide. Under the same conditions, succinic acid gave a mixture of succinimide and succinaminic acid. Thus, for glutaric acid, the reaction takes place according to the scheme:



and for succinic acid



It is of interest to note that in the amidation of succinic acid, a small amount of ammonium sulfate was obtained under conditions which excluded the hydrolysis of sulfaminic acid as a result of the treatment subsequent to the reaction action. The amount of ammonium sulfate fairly accurately corresponds to the yield of succinimide; consequently, the hydrolysis of the sulfaminic acid takes place as a result of the water given off in the formation of the succinimide, according to the scheme:

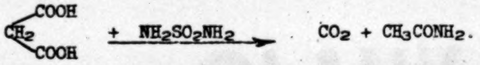


Excess sulfamide probably serves as a source of ammonia for the formation of the neutral salt. It is very possible that this observation may make possible a more detailed analysis of the mechanism of amidation with sulfamide.

The action of two moles of sulfamide on succinic and glutaric acids gives well crystallized, easily water-soluble compounds whose nature has not yet been determined. We have not succeeded in isolating from the products of the reaction any diamides, imides, or aminic acids. It is obvious that sulfamide reacts with imides of glutaric and succinic acids to form more complicated products.

Phthalic acid and phthalic anhydride, under the action of either one or two moles of sulfamide, gives phthalimide in good yield. We did not succeed in obtaining the diamide by the action of sulfamide on phthalic acid.

The action of sulfamide in a solution of pyridine on malonic acid splits off carbon dioxide. If an excess of malonic acid is allowed to act on the sulfamide, then it is easy to separate from the products of the reaction acetamide in a yield of about 88%, based on the amount of sulfamide used. Therefore, the reaction takes place according to the scheme:



If we cause equivalent amounts of malonic acid and sulfamide to react, the yield of acetamide is considerably lower, and if an excess of sulfamide is used, no acetamide can be separated from the reaction products. We expect to give the explanation of this phenomenon in one of our subsequent reports.

Benzylmalonic acid reacts in the same way as malonic acid, but gives much better yields. The reaction of equivalent amounts of sulfamide and benzylmalonic acid in pyridine solution gave 72% of the theoretical amount of the amide of hydrocinnamic acid.

In the reaction of sulfamide on oxalic acid, the evolution of carbon dioxide was observed. No oxamide or oxaminic acid were detected among the reaction products. From these products we isolated a substance with m.p. 179-183°, plus an oily non-crystallizing product, whose nature has not yet been determined. Thus, the direction of the reaction of oxalic acid with sulfamide remains to be explained.

EXPERIMENTAL

Sebacamide from Sebacic Acid

A mixture of 0.005 mole of sebacic acid (1.01 g), 0.015 mole of sulfamide (1.44 g) and 5 ml of dry pyridine was heated for three hours on the boiling water bath. At first everything dissolved. Then the separation of a crystalline precipitate began, its amount gradually increasing. At the end of the reaction the pyridine was driven off in vacuum, and 7.5 ml of a 2 N soda solution was added to the dry residue. The sebacamide was then filtered off with suction and washed with soda. Yield 0.85 g, or about 85% of the theoretical. Recrystallization from alcohol gave fine prisms, m.p. 208° (uncorrected). The compound gave no melting point depression with known sebacamide [2].

Adipamide from Adipic Acid

The reaction and the isolation of the reaction products were conducted in the same way as for sebacic acid. From 0.01 mole of adipic acid (1.46 g), 0.03 mole of sulfamide (2.88 g) and 5 ml of pyridine, 1.19 g of adipamide were obtained, that is, 82% of theory. Recrystallization from water gave a finely crystalline, colorless powder. M.p. 218-220°, (uncorrected). The compound gave no melting point depression with known adipamide [3].

The Reaction of Glutaric Acid with Sulfamide

A. The preparation of glutarimide. A mixture of 0.01 mole of glutaric acid (1.32 g), 0.012 mole of sulfamide (1.15 g), and 3 ml of dry pyridine was heated on the boiling water bath. After three hours of heating, a dense crystalline precipitate formed on the bottom of the flask, and the liquid above it was of a light yellow color. After cooling, 15 ml of 1 N soda solution was added to the reaction mixture, and the pyridine and water were then driven off in vacuum. To the dry precipitate, 10 ml of water was added, and the water was again driven off in vacuum until dryness. The dry residue was extracted eight times with 10 ml portions of boiling benzene. The united benzene extracts were concentrated to dryness on the water bath. The residue was a light yellow oil which soon began to crystallize. The product was squeezed between sheets of filter paper; yield 0.85 g, or 75% of the theoretical, m.p. 152-153°. Recrystallization from alcohol gave fine colorless platelets, m.p. 153-154°; no m.p. depression with known glutarimide [4].

B. The action of 2 moles of sulfamide on glutaric acid. The reaction, and the treatment of the reaction products were carried out under the same conditions and in the same manner as in A. But the sulfamide used was 0.025 mole (2.4 g) per 0.01 mole of glutaric acid. 0.4 g of a viscous oil was obtained, from which a considerable quantity of crystals melting at 62-72° was obtained. The substance has not yet been more thoroughly investigated.

The Reaction of Succinic Acid with Sulfamide

A. The preparation of succinimide and succinaminic acid. 0.03 mole of succinic acid (3.54 g) and 0.033 mole of sulfamide (3.17 g) were mixed with 10 ml of dry pyridine and the mixture was heated on an oil bath at 120-125° for an hour. A transparent solution was first formed, but after 7 minutes a considerable quantity of yellowish fine needles suddenly precipitated, and the reaction mixture turned into a viscous porridge. At the end of the reaction, the pyridine was driven off at 60° in vacuum, and the dry residue was extracted 3 times with 25 ml portions of boiling acetone. We thus obtained precipitate A (see below) and an acetone solution of succinimide and succinaminic acid. After the acetone had been driven off on a water bath, the residue was dissolved in 25 ml of cold acetone, and the solution filtered to remove the small amount of precipitate. The transparent, colorless solution was concentrated in vacuum at 50°; the residue was 3.3 g of an almost colorless viscous oil, easily soluble in water, with a faintly acid reaction by Congo red. After a day, a considerable amount of coarse, long needles separated out. As investigation showed, this oil was a mixture of succinimide and succinaminic acid. In order to separate them, the product was dissolved in 10 ml of water (several hundredths of a gram of grayish tar did not dissolve) and a small amount of activated charcoal was added to the solution, which was then filtered. The colorless solution was accurately neutralized with caustic soda, using phenolphthalein. 15.45 ml of 1 N solution were required, the equivalent of 0.015 mole of succinaminic acid (50% of the theoretical yield). After neutralization, the solution was evaporated to dryness at 40° in vacuum, and the dry residue was twice extracted with 25 ml portions of warm acetone. Precipitate B was thus obtained (see below), plus an acetone solution of succinimide. The acetone was driven off on the water bath to leave 1.2 g of oil, which immediately began to crystallize. The crystals melted at 115-120°. Recrystallization from benzene gave fine, feathery, colorless platelets or bipyramids, m.p. 122.5-124°. This substance gave no melting point depression with known succinimide and had all the properties of succinimide [5]. Thus, the yield of succinimide was about 40% of the theoretical.

Residue A was mixed with 40 ml of absolute alcohol and the insoluble part was filtered off with suction and washed with absolute alcohol. We thus obtained 2.0 g (or about 0.015 mole) of ammonium sulfate, which was identified by its melting point, its qualitative reactions, and a quantitative determination of ammonia and sulfate ion.

> 0.0212 g required 3.22 ml of 0.1 N acid for the neutralization of the ammonia; calculated for ammonium sulfate 3.21 ml.
>
> 0.1724 g gave 0.3038 g of barium sulfate; calculated for ammonium sulfate, 0.3045 g.

The filtrate from the ammonium sulfate showed a sharply acid reaction to Congo red and was not further investigated.

Residue B, consisting chiefly of the sodium salt of succinaminic acid, was twice extracted with 30 ml portions of boiling alcohol, and the small residue was disregarded. Upon cooling, the solution became cloudy, and remained that way for a day. A small amount of activated charcoal was therefore added to it, and the solution was filtered. The colorless solution obtained was evaporated to dryness in vacuum. A thick syrup was obtained as the residue. After two days, this crystallized almost completely in the form of long colorless needles. As the sodium salt of succinaminic acid is not described in the literature, the product was converted into the free acid. It was dissolved in 10 ml of water (a slight cloudiness was removed by the addition of a pinch of activated charcoal, and filtration) and the colorless solution was accurately neutralized with hydrochloric acid using Tropeolin 00. There was an acid reaction after the addition of 13 ml of 1 N hydrochloric acid. This corresponded to 0.013 mole of succinaminic acid, or about 43% of the theoretical amount (*cf.* the first neutralization with alkali, above). After neutralization, the solution was evaporated in vacuum at 30° to dryness, and the residue extracted 3 times with 25 ml portions of boiling acetone. The colorless, transparent acetone solution was concentrated to a volume of about 10 ml. Upon cooling, there precipitated fine colorless needles of succinaminic acid, m.p. 153-154°. Their properties corresponded to those described in the literature [6]. A mixed test with known succinaminic acid gave no depression of the melting point. The yield was 0.7 g of completely purified product. An additional 0.55 g was obtained from the mother liquor, so that in all 1.25 g was obtained, or about 35% of the theoretical yield.

B. The reaction of succinic acid with two molecules of sulfamide was carried out under the same conditions, but with the use of 0.02 mole of succinic acid (2.36 g), 0.04 mole of sulfamide (4.22 g), and 10 ml of dry pyridine. After the flask containing the reaction mixture had been immersed for five minutes in an oil bath heated to 120-125°, a violent effervescence took place and the mixture immediately became viscous as a result of the formation of a crystalline precipitate. The treatment of the reaction mixture was carried out as in case A, up to the point of neutralization with caustic soda, of which only 6 ml of a 1 N solution was needed. The aqueous solution was evaporated to dryness at 40° in vacuum, and the dry residue was extracted twice with 25 ml portions of boiling acetone. After cooling, the acetone extracts were filtered from a very small quantity of precipitate which had formed, and evaporated to dryness on a water bath. The residue contained 2.0 g of a light yellow oil. After a day, this crystallized. The crystals, which were fine needles, were pressed between filter papers. This gave 1.1 g of a crystalline substance with m.p. 80-86°. Recrystallization from boiling benzene gave fine branched needles, m.p. 96-98° (uncorrected). The melting point was unchaged after repeated recrystallization. The nature of this substance is being studied.

The Amidation of Phthalic Acid and Phthalic Anhydride

A. A mixture of 0.01 mole of phthalic acid (1.66 g), 0.012 mole of sulfamide (1.15 g) and 5 ml of pyridine was heated for three hours on a boiling water bath. During the heating, a crystalline precipitate gradually formed. At the end of the reaction, the pyridine was distilled off in vacuum to give a dry residue, which was treated with 5 ml of 2N soda solution. This solution was again evaporated in vacuum to dryness, and 5 ml of water was added to the residue. The phthalimide was then filtered off with suction and washed with water. Yield 1.46 g, i.e., about 88% of the theoretical amount. After recrystallization from water, the melting point was 235-236° (uncorrected). The properties corresponded to those described in the literature [7]. If a larger amount of sulfamide was used in the reaction (0.03 mole per 0.01 mole of acid) the yield of phthalimide fell to 80% of the theoretical, and it was possible to obtain from the mother liquor a substance with m.p. 169-172°, whose nature has not yet been determined.

B. The reaction of phthalic anhydride with sulfamide was carried out under the same conditions and with molecular ratios of 1:1.2 and 1:3. In both cases phthalimide was obtained in yields of 80 to 82% of the theoretical amount.

The Amidation of Malonic Acid

A mixture of 0.01 mole of malonic acid (1.04 g), 0.005 mole of sulfamide (0.49 g), and 5 ml of dry pyridine was heated on a boiling water bath. After several minutes, there was a copious evolution of gas, which was identified as carbon dioxide. After 30 minutes, the transparent solution became cloudy, and gave a crystalline precipitate. The reaction mixture was heated for three hours and 10 ml of 1 N soda solution was then added. The pyridine and water were driven off in vacuum at 35°. The dry residue was extracted three times with 10 ml portions of acetone. The acetone was driven off, and the liquid residue was placed in a desiccator over sulfuric acid. After a day, a trace of acetamide was added. The substance immediately crystallized completely. The crystals melted at 78-81°. A mixed test with a known sample of acetamide melted at 79-81°. Yield 0.26 g, or about 88% of the theoretical amount, basing the calculation on the sulfamide, and about 44%, basing the calculation on the malonic acid.

The Amidation of Benzylmalonic Acid

This experiment was carried out in the same way as the amidation of malonic acid. For the reaction, we used 0.005 mole of benzylmalonic acid (0.97 g), 0.006 mole of sulfamide (0.58 g), and 3 ml of dry pyridine.. During the reaction, the evolution of carbon dioxide took place. After neutralization with soda and evaporation to dryness in vacuum, the dry residue was extracted 3 times with 10 ml portions of alcohol. The united alcohol extracts were evaporated on a boiling water bath. The residue gave 0.7 g of the crystalline amide of hydrocinnamic acid. After recrystallization from water, colorless needles were obtained with m.p. 102-103°. The substance gave no depression of the melting point when mixed with the known amide of hydrocinnamic acid [8].

The reaction of oxalic acid with sulfamide was carried out several times under various conditions. No oxamide or oxaminic acid was found among the products of the reaction. One of the most characteristic experiments will be described. A mixture of 0.01 mole of oxalic acid (0.9 g), 0.01 mole of sulfamide (0.96 g), and 3 ml of pyridine was heated on a boiling water bath. After 40 minutes of heating, everything went into solution, and there took place a voluminous evolution of gas, which was identified as carbon dioxide. After an hour's heating, the formation of a crystalline precipitate began. After three hours of heating, 10 ml of a 1 N solution of soda was added to the gruel-like crystalline mass.

Part of the precipitate did not dissolve during this (about 0.2 g). The substance was filtered off with suction and washed with water. Its m.p. was 170-183°, its reaction neutral. The filtrate was evaporated to dryness in vacuum and the residue extracted twice with 10 ml portions of alcohol. The alcohol was driven off to leave 0.15 g of an oily liquid, which did not crystallize after standing for several months. The residue which was insoluble in alcohol was a colorless substance with a far from sharp melting range of 196-220°. This was not investigated in greater detail.

SUMMARY

It has been shown that in the amidation with sulfamide of dibasic carboxylic acids with carboxyl groups far apart, good yields of the acid diamides are obtained. The amidation of phthalic and glutaric acids gives the corresponding cyclic imides. The amidation of succinic acid gives a mixture of succinimide and succinaminic acid, and with an excess of sulfamide, gives a substance whose nature has not yet been determined. The amidation of malonic and benzylmalonic acids results in the splitting off of carbon dioxide and the formation of the amides of the corresponding monobasic acids.

The amidation of oxalic acid results in the evolution of carbon dioxide and the formation of a compound whose nature has not yet been determined.

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*See CB translation p. a-675.

ON THE ALKALOIDS OF THALICTRUM MINUS L.

III. ON THE ALKALOIDS OF THE RANUNCULACEAE FAMILY

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For as long as the genera Aconitum and Delphinium (fam. Ranunculaceae) have been the subjects of investigation, up to the present time, although many interesting alkaloids have been isolated [1], our knowledge of the alkaloids of the genus Thalictrum* of this family (delphinium) has remained extremely limited.

There is a certain amount of very incomplete data only about the alkaloids of Thalictrum macracarpum and Th. flavum. From the roots of Thalictrum macracarpum the crystalline base thalictrin [2] was isolated in 1880. Not even the melting point and the general formula were found for this compound. Apparently the poisonous effect of thalictrin approximates that of aconitine. There is also an indication that berberine [3] is present in Thalictrum flavum.

Finally, in 1931, the alkaloid department of the Scientific Chemical-Pharmaceutical Institute undertook a preliminary investigation of the roots of Th. minus L, Th. petaloideum, and Th. simplex. One of these species (the particular one was not mentioned) gave a crystalline alkaloid [4]. Unfortunately, neither the elementary composition nor the physico-chemical properties of this alkaloid were given.

We suggest that all this work on the investigation of the Thalictrum genus requires confirmation by repetition, and greater precision.

In the territory of the USSR, there grow 19 species of Thalictrum. Of these, 8 are distributed throughout Central Asia [5]. All the species of Thalictrum, as well as of Aconitum and Delphinium, contain alkaloids.

Along with other genera of the crowfoot family, we began to investigate all the species of Thalictrum which are distributed in Central Asia. We investigated, at different stages of the growing season, two species: Th. sultanbadense Stapf, which at the beginning of the fruit bearing period contains in the above-ground portions 0.2% of alkaloids, and Th. minus L. [6]. The latter was subjected to a more detailed investigation. Each organ was investigated individually at different stages of development.

In the present communication we shall present more detailed data on the investigation of the parts of Thalictrum minus L. which grow above ground and of the roots, prepared at a single stage of growth, and in particular at the beginning of the formation of the ovaries (24th to 30th of May), as well as of the roots of Th. minus L. dug up at the end of the period of vegetation (13th to 19th of October). This material was collected by us in 1946 on the northern slope of the Kuraminsk Range (from the Pangas Pass along the Lyashkarak, Tashkent region).

The parts of the plant growing above ground were crushed and moistened with ammonia, and then exhaustively extracted with dichloroethane. The total amount of alkaloid obtained was 0.41% of the weight of the dry plant. When the mixture of bases was treated with alcohol at 30°, part went into solution and part was insoluble. The latter was in the form of a yellow-green powder with m.p. 247-249°. The yield was about 33% of the total amount of alkaloids. This base was purified by the formation of the hydrochloride, the base being then obtained from it again and recrystallized from a mixture of alcohol and chloroform. The melting point thus rose to 252-253° (with decomposition).

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* From the Greek, thalictron, name of some sort of medicinal plant of the Dioscarides.

$[\alpha]_D = -64.5°$. Upon further recrystallization from alcohol, chloroform, and ether, the melting point and the rotation remained unchanged, while the light yellow color of the crystals was maintained through every recrystallization. An elementary analysis of the base led to the general formula $C_{20}H_{23}O_3N$.

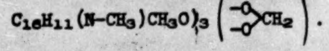
As this alkaloid appeared different from all the other bases hitherto described in the literature, we called it thalmin. A determination of the functional groups showed that its formula could be partially broken down in the following manner: $C_{17}H_{14}O(N{-}CH_3)(CH_3O)_2$.

The function of the third oxygen has not yet been determined. We could obtain no qualitative reactions for ketone or aldehyde groups. Thalmin is an unsaturated alkaloid. It forms a well crystallized hydrochloride, perchlorate, and methyliodide. As the latter was formed at the first stage of methylation, it may be assumed that the nitrogen is tertiary.

The portion easily soluble in alcohol was cooled to -10° and the alcohol then slowly removed by evaporation at 20-30°. A crystalline base suddenly precipitated out, with m.p. 192-193°; $[\alpha]_D = +252.9°$. The yield was about 15% of the total amount of alkaloids. Further cyrstallization from various solvents changed neither the melting point nor the rotation. On the basis of an elementary analysis, we determined the composition of this alkaloid to be $C_{21}H_{25}O_4N$, and gave it the name thalmidin. The nitrogen of this alkaloid is tertiary, and at the first stage it forms a crystalline methyliodide which melts at 254-255° (with decomposition). Thalmidin is unsaturated. Two oxygens are in methoxyl groups, but the functions of the other two oxygens has not yet been determined. No aldehyde, ketone, or methylenedioxy groups have been detected. The formula can be broken down into: $C_{18}H_{13}O_2(N{-}CH_3)(CH_3O)_2$.

The isolation of alkaloids from the roots of Thalictrum minus L. (collected in May) was carried out by means of a 7-fold extraction with dichloroethane. The base was extracted from dichloroethane with 10% sulfuric acid. The acid solution was made alkaline with gaseous ammonia (with cooling) and exhaustively extracted with ether and then dichloroethane. After removal of the solvent, a total of 0.95% of alkaloid was obtained (0.77% from the ether and 0.18% from the dichloroethane), based on the weight of the dry roots. The separation of the alkaloids in the ether extract was carried out by means of the separation, in sequence, of the hydrochloride and tartrate. When the alkaloid mixture was treated with 5% hydrochloric acid, it gave a crystalline hydrochloride (26.8%) with m.p. 254-256°. After recrystallization from water, the melting point rose to 268-270°. The hydrochloride gave a base with m.p. 137-138°, $[\alpha]_D = +255.3°$, named by us thalicmin. The yield of thalicmin was 17.5% of the original total. An elementary analysis of the base and a determination of the molecular weight lead to the formula $C_{21}H_{25}O_5N$.

Thalicmin forms well crystallized salts. We obtained the hydrochloride, hydrobromide, hydriodide, and methyliodide. The nitrogen of thalicmin is tertiary, and forms a methyliodide in the first stage of methylation. In the thalicmin molecule, two oxygens form a methylenedioxy group, and the three remaining ones are in the form of methoxyls. The formula of this alkaloid can be broken down as:



$$C_{16}H_{11}(N\text{-}CH_3)CH_3O)_3\left(\begin{matrix}-O\\-O\end{matrix}\!\!>CH_2\right).$$

From the hydrochloride mother liquors, after the hydrochloride of thalicmin was separated, a mixture of bases was obtained, from which the tartrate was precipitated. The tartrate was purified by recrystallization until the m.p. was constant at 239-240°. The tartrate gave a crystalline base with m.p. 192-193°, $[\alpha]_D = 84.05°$. We gave this the name thalicmidin. The yield of thalicmidin was 6.75% of the original total of alkaloids. An elementary analysis of thalicmidin led to the general formula $C_{20}H_{25}O_4N$. We obtained in crystalline form the tartrate, hydroiodide, and methyliodide. The latter formed at the first stage of methylation, indicating the tertiary character of the nitrogen. Thalicmidin is unsaturated, and contains three methoxyl groups. No ketone, aldehyde, or methylenedioxy groups were detected qualitatively. The function of the fourth oxygen is still undetermined, but we can break down the formula of thalicmidin in the following fashion: $C_{16}H_{13}O(N\text{-}CH_3)(OCH_3)_3$.

The dichloroethane extract (0.18%) gave an orange crystalline base No. 5, with m.p. 243°. The roots of Th. minus L. of the autumn collection gave almost the same amounts of the same alkaloids as were obtained from the previous collection.

Thus, from the entire plant of Thalictrum minus L. we obtained 5 alkaloids in crystalline form:

1) $C_{20}H_{23}O_3N$, thalmin: $C_{17}H_{14}O(N\text{-}CH_3)(CH_3O)_2$
2) $C_{21}H_{25}O_4N$, thalmidin: $C_{18}H_{18}O_2(N\text{-}CH_3)(CH_3O_2)_2$ } from above ground portion

3) $C_{21}H_{25}O_5N$, thalicmin: $C_{16}H_{11}(N\text{-}CH_3)(CH_3O)_3(CH_2O_2)$.
4) $C_{20}H_{25}O_4N$, thalicmidin: $C_{16}H_{13}O(N\text{-}CH_3)(CH_3O)_3$
5) Base No. 5 – orange crystals with m.p. 243°. } from roots

A comparison of the partially broken down formulas of all four alkaloids made it fairly easy to see that they were all derivatives of very closely related basic skeletons. If we assume that all the oxygens whose functions were not determined were attached to carbon and formed substituent groups, then all the compounds can be referred to a single carbon skeleton, C_{16}. As is well known, in such comparatively high molecular weight compounds, it is difficult to determine the amount of hydrogen with any accuracy simply on the basis of elementary analysis. Therefore a discrepancy of one or two hydrogens can be considered as possible within the limits of error of the analysis. If we imagine that all the substituent groups are replaced by hydrogen, then the fundamental nuclei of these alkaloids have the formulas $C_{16}H_{15}(N\text{-}CH_3)$ – benzyltetrahydroisoquinoline, and $C_{16}H_{14}(N\text{-}CH_3)$ – aporphine or alkaloids of the type of morphine and thebaine. This comparison of the gross formulas for the fundaments skeletons of these bases with the nuclear compositions of the groups of alkaloids being investigated leads us to the thought that our new alkaloids are also constructed along the same lines. Comparing the formula of thalicmin with that of armepavine, which has been demonstrated by us to be a derivative of benzyltetrahydroisoquinole [7], it is easy to see that they are completely analogous and are both derived from a fundamental compound with the composition $C_{17}H_{19}N$, or $C_{16}H_{16}(NCH_3)$:

$C_{16}H_{11}(NCH_3)(OCH_3)_3(CH_2O_2)$ thalicmin,
$C_{16}H_{13}(NCH_3)(OCH_3)_2(OH)$ armepavine.

In addition, we have obtained with regard to thalicmin a certain amount of preliminary experimental data confirming this opinion.

Gadamer [6] found that a characteristic peculiarity of tetrahydroisoquinoline was their ability to react with acid chlorides and acid anhydrides (chlorocarbonic ester, acetyl chloride, and acetic anhydride) by rupturing the hydrogenated heterocyclic ring to form urethane derivatives, losing their basic properties and their optical activity. An experiment carried out with thalicmin showed that under the action of acetyl chloride this too formed a crystalline substance with m.p. 191-192°, lacking basic properties and optical activity. This fact very probably is enough to classify thalicmin with the benzyltetrahydroisoquinoline series.

The work to elucidate the structure of the newly discovered alkaloids, and the investigation of the mother liquors are being continued.

EXPERIMENTAL

The Isolation of the Group of Alkaloids

29.5 kg of air-dried crushed plant Thalictrum minus L. (the above-ground portions) was moistened with 10% ammonia. Dichloroethane was allowed to percolate through it 11 times. Each time the base was thoroughly removed from the extract with 10% sulfuric acid. The acid solution was cooled and saturated with gaseous ammonia till it gave a strongly alkaline reaction. The yellowish-green amorphous precipitate which formed was filtered off with suction, washed with water, and dried in vacuum. A total of 112.5 g of alkaloids was obtained. The aqueous mother liquor was extracted with dichloroethane. The dichloroethane solution was dried over calcined sodium sulfate and concentrated to a small volume, then transferred a beaker, and the solvent completely volatilized. 8.7 g of a black, hard, tarry mass was obtained. When this was crushed to give a powder, the color was yellowish-green.

The total yield of all the alkaloids was 121.2 g, amounting to 0.41% of the weight of the dry plant.

The Isolation of Alkaloids From the Group

121.2 g, the total of alkaloids, was first treated at 30° with a liter of alcohol, and then, twice more, successively, with 500 ml portions. After filtration with suction, there remained an insoluble precipitate (B), 40 g of crude thalmin, which was in the form of a yellowish-green powder with m.p. 247-249° (with decomposition). The alcoholic solution was (A).

Thalmin Hydrochloride

40 g of crude thalmin was dissolved in 5% alcoholic hydrochloric acid. A very small part did not dissolve. The solution was filtered and evaporated at 30° When the alcohol was slowly driven off, there separated fine yellowish crystals of the hydrochloride, which were filtered with difficulty from the mother liquor. They darkened and deliquesced in the air. After drying, they melted at 147-157° (with decomposition).

Thalmin

The aqueous solution of thalmin hydrochloride was saturated with cooling with gaseous ammonia. The yellow amorphous base was filtered off with suction, washed with water, and dried in vacuum. Recrystallization from a mixture of chloroform and alcohol gave yellow crystals with m.p. 252-253° (with decomposition).

The alcoholic mother liquor of the hydrochloride was saturated with gaseous ammonia (with cooling). During this process, the base, the moment it was set free, dissolved in the alcohol, from which crystalline thalmin precipitated. The crystals were washed with alcohol and water. The dried crystals were yellow, and melted at 252-253° (with decomposition).

Thalmin was recrystallized from various solvents (chloroform, alcohol, ether, acetone, etc.) to give a crystalline yellow base with m.p. 252-253° (with decomposition).

Thalmin is soluble with difficulty in methyl, ethyl, and amyl alcohols, and in acetone, benzene, toluene, gasoline, carbon tetrachloride, and butyl acetate; it dissolves easily in chloroform; it is insoluble in water and in alkalies.

0.1506 g substance: 14.0 ml chloroform, $\underline{l} = 1$ dm.
$\alpha = -0.6938°$; $[\alpha]_D = 64.5°$.
0.1285 g substance: 0.3476 g CO_2; 0.0790 g H_2O.
0.1244 g substance; 4.9 ml N_2 (18°, 721.6 mm).
0.1076 g substance: 4.9 ml N_2 (18°, 718.1 mm).
0.0258 g substance: 7.4 ml 0.1 $\underline{N}$ $Na_2S_2O_3$.
0.0222 g substance: 6.45 ml 0.1 $\underline{N}$ $Na_2S_2O_3$.
Found %: C 73.71; H 6.81; N 4.35, 4.32.
CH_3O 14.83, 15.02.
$C_{20}H_{23}O_3N$. Computed %: C 73.84; H 7.07; N 4.31; CH_3O 19.05.

Thalmin methyliodide

To 2 g of crystals of the base, 20 ml of methyl alcohol was added and 4 ml of methyl iodide. All the crystals went into solution during the first hour. The mixture was heated for 6 hours. The methanol and the excess of methyl iodide were then distilled off on a water bath until the volume was reduced to 5 ml. Upon standing, a tarry orange-colored mass precipitated. The methanol was decanted off and 38 ml of ethyl alcohol was added to the tar. Upon rubbing with a glass rod, the tar gradually turned into a powder. Upon heating with additional alcohol under a reflux condenser, the entire mass dissolved. The crystals which precipitated out were filtered off with suction and the mother liquor concentrated. Two recrystallizations from alcohol gave crystals with a faint orange color and a melting point of 250° (with decomposition). Yield of methyliodide 1.8 g.

0.1442 g substance: 2.9 ml 0.098 $\underline{N}$ $AgNO_3$.
0.1214 g substance: 2.25 ml 0.1033 $\underline{N}$ $AgNO_3$.
Found %: I 24.31, 24.31.
$C_{20}H_{23}O_3N \cdot CH_3I$. Computed %: I 26.6.

Thalmin perchlorate

. A saturated aqueous solution of ammonium perchlorate was added to an aqueous solution of thalmin hydrochloride. A light-colored flocculent precipitate settled out. This was filtered with suction and washed with water. Recrystallization from alcohol gave fine crystalline needles, growing out from a center, and slightly yellowish in color. M.p. 238-241° (with decomposition).

Thalmidin

From 2 liters of the alcoholic solution (A), cooling to -10° caused to precipitate out 5.6 g of crystals. An additional 8.4 g precipitated out when the solvent was distilled off from the mother liquor. Thus a total of 14.0 g of crystalline thalmidin was obtained, with m.p. 192-193° (with decomposition). When the 14 g of crude thalmidin was recrystallized from alcohol (1:25), fine yellowish crystals precipitated out. These were filtered with suction and washed with ether. The crystals had a silvery luster and melted at 192-193° (with decomposition). Their melting point remained unchanged upon further recrystallization from various solvents.

Thalmidin is easily soluble in chloroform, alcohol, methanol, and acetone, soluble with more difficulty in ether, insoluble in water and in alkalies.

0.3155 g substance: 20 ml chloroform; $\underline{l} = 2$ dm;
$\alpha = +7.98°$; $[\alpha]_D = +252.2°$.
0.0912 g substance: 0.2360 g CO_2; 0.0567 g H_2O.
0.1422 g substance: 4.8 ml N_2 (18°, 727.2 mm).
0.1140 g substance: 4.0 ml N_2 (16°, 724.0 mm).
0.0278 g substance: 10.45 ml 0.1 $\underline{N}$ $Na_2S_2O_3$.
Found %: C 70.80; H 6.95; N 3.76, 3.88;
CH_3O 19.44
$C_{21}H_{25}O_4N$. Computed %: C 70.98; H 7.04; N 3.93; CH_3O 17.46.

Thalmidin methyliodide

5 ml of methyl alcohol and 1 ml of methyl iodide were added to 0.5 g of crystals of the base. The mixture was boiled for 6 hours. After the methyl iodide had been driven off along with the methanol, an oily mass remained, which was crystallized from a mixture of alcohol and acetone. The methyliodide crystals were filtered off with suction and washed with acetone. M.p. 254-255° (with decomposition).

Separation of total alkaloids from the roots of *Thalictrum minus* L.

18 kg of air-dried, finely crushed roots of *Thalictrum minus* L. (May collection) were moistened with 10% ammonia, placed in a percolator, and thoroughly extracted with dichloroethane (7 times). The dichloroethane solution was extracted with 10% sulfuric acid until the alkaloids were completely removed. During cooling in the presence of ether, the acid solution was neutralized with gaseous ammonia until an alkaline reaction was obtained. The moment the alkaloids were set free, they went into the ether. The ether solution was removed, and the aqueous solution was then thoroughly extracted first with ether and then with dichloroethane. The solutions obtained were dried over calcined potash. The solutions were concentrated to a small volume and transferred to a beaker. Drying in vacuum gave: from the ethereal solution 143.5 g (0.77% of the weight of the roots); from the dichloroethane solution, 32 g (0.18%).

Thus 175.5 g of total alkaloids were obtained, corresponding to 0.95% of the weight of the roots.

The Fractionation of the Alkaloid Mixture

Thalicmin hydrochloride

To 143.5 g of total alkaloids (ether extract) there was added 420 ml of 5% hydrochloric acid. The hydrochloride formed as a gel, but upon rubbing with a glass stirring rod, it was transformed into a finely crystalline form. After being allowed to stand for 18 hours, the precipitated hydrochloride was filtered with suction, and washed with water and ether. The crude hydrochloride was dried in vacuum to constant weight (38.5 g). It had m.p. 254-256° (with decomposition). Recrystallization from water (1:14) gave 16.8 g of crystalline hydrochloride, with the constant m.p. 268-270° (with decomposition in a sealed capillary). The mother liquor gave an additional 1.9 g of crystalline hydrochloride with m.p. 265-268° (with decomposition).

The mother liquor was then neutralized, during cooling, with gaseous ammonia dissolved in ether. The base was thoroughly extracted with ether. After drying over potash, the solvent was removed to give a mixture of alkaloids, from which an additional 5.2 g of hydrochloride with m.p. 254-258° was obtained.

The hydrochlorides obtained from the mother liquors were united and recrystallized from water until the m.p. reached 268-270°. The yield of crystalline hydrochloride with m.p. 268-270° was 20.8 g. Upon standing in thelight, the hydrochloride crystals changed on the surface, and acquired a brownish color.

Thalicmin

The hydrochloride was treated with 25% ammonia to give the amorphous base with m.p. 124-125°. Recrystallization from methanol (1:14) gave crystalline thalicmin with m.p. 137-138°. The total yield of thalicmin was 25.1 g (17.5% of the original total alkaloids).

Thalicmin dissolved readily in chloroform, alcohol, methanol, and acetone; it was less soluble in ether, benzene, and carbon tetrachloride, and insoluble in water and in alkalies.

0.1684 g substance: 25 ml absolute alcohol: l = 1 dm;
$\alpha = +1.72°$; $[\alpha]_D^{24} = +255.3°$.
0.1228 g substance: 0.3102 g CO_2; 0.0736 g H_2O.
0.1230 g substance: 0.3072 g CO_2; 0.0736 g H_2O.
0.1250 g substance: 0.3122 g CO_2; 0.0728 g H_2O.
0.1464 g substance: 5.45 ml N_2 (27°, 718.7 mm).
0.1460 g substance: 5.40 ml N_2 (26°, 718.06 mm).
0.0254 g substance: 12.4 ml 0.1 N $Na_2S_2O_3$.
0.0214 g substance: 10.4 ml 0.1 N $Na_2S_2O_3$.
0.1196 g substance: 3.285 ml 0.1 N H_2SO_4.
Found %: C 68.94, 68.16, 68.15; H 6.71, 6.69, 6.55; N 3.85, 3.85; CH_3O 25.24, 25.13; M 363.5.
$C_{21}H_{25}O_5N$. Computed %: C 68.88; H 6.79; N 3.77; CH_3O 25.05; M 371.2

Thalicmin hydriodide

0.5 g of the base was dissolved in 20 ml of alcohol, and aqueous hydriodic acid was added to the solution drop by drop until Congo red showed a weakly acid reaction. During this process, the crystalline hydriodide precipitated. The crystals were filtered with suction and washed with 20 ml of alcohol. The hydriodide was recrystallized from alcohol (1:220 to give fine white needle-shaped crystals, which were filtered with suction and washed with alcohol. The hydriodide had m.p. 210-215° (with decomposition) and 223-224° (with decomposition) in a sealed capillary.

0.1143 g substance: 2.22 ml 0.1 N $AgNO_3$.
Found %: I 24.67; M 514.8.
$C_{21}H_{25}O_5N \cdot HI$. Computed %: I 25.43; M 499.1.

Thalicmin hydrobromide

1 g of the base was dissolved in methanol and aqueous hydrobromic acid was added to the solution drop by drop until there was a weakly acid reaction. The thalicmin hydrobromide crystals formed were filtered with suction and washed with water. The hydrobromide recrystallized from water had m.p. 258-260°.

The hydrobromide gave a base with m.p. 137-138°. A mixed test with thalicmin gave no lowering of the melting point.

Thalicmin methyliodide

To 0.5 g of thalicmin there was added 5 ml of methanol and 1 ml of methyl iodide. The mixture was heated with a reflux condenser to the boiling point. At first everything dissolved. Then after 5 minutes the crystalline methyliodide formed. The boiling was continued for 35 minutes, and the crystals were then filtered with suction, washed with methanol, and dried. 0.6 g of crystals with m.p. 226-227° was obtained. The methyliodide was recrystallized twice from water, (1:80). The melting point was thus raised to 231-232°, and 236-237° (sealed capillary). The addition of 25% ammonia did not change the melting point of the methyliodide crystals. This indicated that the methyl iodide had added on to the tertiary nitrogen.

0.1058 g substance: 2.08 ml 0.1 N $AgNO_3$.
Found %: I 24.99; M 508.2
$C_{21}H_{25}NO_3 \cdot CH_3I$. Computed %: I 24.84; M 513.14.

The acetylation of thalicmin

In a glass tube sealed at one end 1 g of the base was placed. To this there was added 10 ml of acetyl chloride. The other end of the tube was quickly sealed, and the contents carefully shaken. A strong evolution of small bubbles was first observed. The entire mass gradually dissolved, and a precipitate soon formed. After 12 days, the tube was opened. The acetyl chloride was driven off in vacuum. The weight of the product obtained was 1.2 g, the m.p. 216-217°. The acetylated product was treated with 20% ammonia. The acetylated base was filtered with suction, washed with water, and dried in vacuum. M.p. 120-124°. At 140° it again solidified, and it melted again at 165-166°. The amorphous mass was recrystallized twice from alcohol (1:10). 0.9 g of crystalline acetylated thalicmin was obtained, m.p. 191-192°; no m.p. depression with thalmidin.

The acetylated thalicmin was optically inactive.

Treatment of the hydrochloride mother liquor

After the thalicmin hydrochloride had been removed, the 500 ml of mother liquor remianing was saturated with gaseous ammonia until the reaction was alkaline. During this process, an amorphous precipitate with a brown color separated out. This was filtered with suction, washed with water, and dried to constant weight (74.4 g).

To the 74.4 g of mixed bases there was added with constant stirring, small portions of a saturated alcoholic solution of tartaric acid, until there was a weakly acid reaction.

This caused the precipitation of an amorphous mass, which was filtered with suction and washed with alcohol. The tartrate was recrystallized from 50% alcohol (1.9 1). The crystals which precipitated out were allowed to stand for a day, and then filtered with suction and washed with alcohol. 18.1 g were obtained, with m.p. 239-240° (with decomposition in a sealed capillary).

The alcoholic mother liquor was concentrated in vacuum to a volume of 755 ml, transferred into a beaker, and evaporated in the air. The crystals which precipitated out were filtered with suction, washed with alcohol, and dried in a vacuum to constant weight (16.3 g). M.p. 230-235° (with decomposition) and 239-240° (with decomposition in a sealed capillary).

Upon standing in the light, the tartrate crystals turned a brownish color.

Thalicmidin

17 g of the tartrate was placed in a mortar, and carefully ground with 20% ammonia. After standing for 2 hours, the base was filtered off with suction, washed with water, and dried in vacuum. The weight of base obtained was 15.2 g, m.p. 180-185°.

The crude thalicmidin was recrystallized twice from methyl alcohol (1:5). The crystals were well formed; they were fine, colorless little needles (a fibrous mass). The dried thalicmidin had m.p. 192-193°. Yield 9.7 g (6.75% of the original total alkaloids).

A mixed test with thalmidin and acetylthalicmin gave lowerings of the melting point.

Upon recrystallization from various solvents, the melting point of thalicmidin remained unchanged.

Thalicmidin was easily soluble in chloroform, alcohol, methanol, and acetone; soluble with more difficulty in ether; insoluble in water and in alkalies.

0.1627 g substance: 25 ml absolute alcohol, $\underline{l} = 1$ dm;
$\alpha = -0.547°$; $[\alpha]_D^{24} = -84.05°$.
0.1236 g substance: 0.3170 g CO_2; 0.0790 g H_2O.
0.1220 g substance: 0.3132 g CO_2; 0.0778 g H_2O.
0.1512 g substance: 6.2 ml N_2 (29°, 717.09 mm).
0.1404 g substance: 5.6 ml N_2 (27°, 719.57 mm).
0.0254 g substance: 13.1 ml 0.1 $\underline{N}$ $Na_2S_2O_3$.
0.0246 g substance: 12.85 ml 0.1 $\underline{N}$ $Na_2S_2O_3$.
Found %: C 69.99, 70.06; H 7.15, 7.14; N 4.19, 4.14;
CH_3O 26.67 27.01.
$C_{20}H_{25}O_4N$. Computed %: C 69.97; H 7.29; N 4.07; CH_3O 27.12.

The qualitative reactions for aldehyde, ketone, and methylenedioxy groups were negative.

Thalicmidin hydriodide

0.5 g of thalicmidin was dissolved in 15 ml of alcohol and an aqueous solution of hydriodic acid was added drop by drop until the reaction was faintly acid. After 5 minutes the mass began to crystallize in the form of fine little needles. The solution was deeply colored. The crystals were filtered off with suction and washed with alcohol. The dried crystals melted at 205-217° (with decomposition), and 222-226° (with decomposition in a sealed capillary). The melting point remained unchanged after repeated crystallization.

Thalicmidin methyliodide

To 0.5 g of the base there was added 10 ml of methanol and 1 ml of methyl iodide. The mixture was boiled with a reflux condenser for 4 hours. The solution was deeply colored. After the methyl iodide had been driven off along with the methanol, a tarry mass remained. This was rubbed and washed with acetone. The yield of dry crude methyliodide was 0.55 g, m.p. 217°. The crude product was recrystallized from water and then from alcohol (1:42). Yield 0.4 g, m.p. 217-217.5°.

0.1071 g substance: 3.8 ml 0.1 $\underline{N}$ $AgNO_3$.
Found %: I 23.08.
$C_{20}H_{25}O_4N \cdot CH_3I$. Computed %: I 26.83.

Base No. 5.

32 g of the total alkaloids (dichloroethane extract) were subjected to treatment first with boiling alcohol and then with acetone. The part that remained insoluble after this treatment was recrystallized from chloroform and ether.

The crystalline base No. 5 was obtained. It had an orange color and a melting point of 243°.

Investigation of the roots of Thalictrum minus L., (autumn crop)

17 kg of the roots of *Thalictrum minus* L. (October crop) gave 141.9 g of total alkaloids (0.83% of the weight of the roots). The ether extract gave 116.9 g (0.68%) and the dichloroethane 25 g (0.15%).

17.65 g of thalicmin (15.17% of the original total alkaloids), 8.55 g of thalicmidin (6.02%) and some base No. 5 were obtained.

SUMMARY

1. The parts of Thalictrum minus L. growing above ground, collected at the end of the flowering period, gave 0.41% of total alkaloids.

When the alkaloids of this mixture were separated, 2 new bases were obtained in crystalline form: thalmin, $C_{20}H_{23}O_3N$, with m.p. 253°, $[\alpha]_D$ -64.5°; and thalmidin, $C_{21}H_{25}O_4N$, with m.p. 192-193°, $[\alpha]_D$ + 252.9°.

2. The roots of Thalictrum minus L., from the spring and the autumn collections, gave 0.95 and 0.83%, respectively.

When the alkaloids of this mixture were separated, 3 alkaloids were obtained in crystalline form: thalicmin, $C_{21}H_{25}O_5N$, with m.p. 137-138°, $[\alpha]_D$ + 255.3°; thalicmidin, $C_{20}H_{25}O_4N$, with m.p. 192-193°, $[\alpha]_D$ -84.05°, and base No. 5, orange crystals with m.p. 243°.

3. A quantitative determination of the functional groups permitted us to give the following breakdown of the formulas:

Thalmin....... $C_{17}H_{14}O(N{-}CH_3)(CH_3O)_2$,
Thalmidin..... $C_{18}H_{16}O_2(N{-}CH_3)\ (CH_3O)_2$,
Thalicmin..... $C_{16}H_{11}(N{-}CH_3)(CH_3O)_3(CH_2O_2)$,
Thalicmidin... $C_{16}H_{13}O(N{-}CH_3)(CH_3O)_3$.

4. Acetylation of thalicmin gave a crystalline, optically inactive derivative with m.p. 191-192°.

5. With the exception of base No. 5, all the alkaloids isolated easily formed crystalline salts and methyliodides.

All 4 alkaloids are probably derivatives of tetrahydriosoquinoline. Thalicmin appears to be N-methylbenzyltetrahydroisoquinoline.

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*See CB translation p. 855 ff.

THE ACTION OF CARBON TETRACHLORIDE

ON THE ESTERS OF PARA-TOLYLPHOSPHINOUS ACID

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In 1945 one of the present authors for the first time [1] investigated the action of carbon tetrachloride on alkyl esters of phosphorous and phenylphosphinous acids. By means of this investigation, we determined that the esters of phosphorous acid, when heated slightly, and the esters of phenylphosphinous acid even at room temperature, react with carbon tetrachloride and give, with the former, esters of trichloromethylphosphinic acid, and with the latter esters of phenyltrichloromethylphosphinic acid.

In the present work we investigated the action of carbon tetrachloride on the various alkylated esters of p-tolylphosphinous acid.

In 1882, for the first time, Michaelis and Paneck [2] found that the reaction of sodium ethylate on p-tolyldichlorophosphine gave the ethyl ester of p-tolylphosphinous acid, with b.p. 240°.

We obtained the alkylated esters of p-tolylphosphinous acid by the action of the corresponding alcohols on p-tolyldichlorophosphine in the presence of dimethylaniline.

Some of the experimental data on the alkylated esters of p-tolylphosphinous acid obtained by us are listed in Table 1.

TABLE 1

No. of compound	Compound	B.P. at 6-13 mm	d8	n_D
1	$C_7H_7P(OCH_3)_2$	107-109°	1.0709	1.5325
2	$C_7H_7P(OC_2H_5)_2$	123-125°	1.0380	1.5138
3	$C_7H_7P(OC_3H_7)_2$-n	129-130°	1.0091	1.5070
4	$C_7H_7P(OC_4H_9)_9$-n	170-171°	1.9899	1.5024
5	$C_7H_7P(OC_4H_9)_2$-iso ...	155-156°	1.9807	1.4987

The esters were mobile, colorless liquids with very unpleasant odors, and distilled in vacuum without decomposition. Under the action of water they hydrolyzed to form p-tolylphosphinous acid. As derivatives of trivalent phosphorus, they reacted, with the evolution of heat, with monohalides of copper and with alkyl halides.

We investigated the action of methyl iodide on various newly synthesized esters of p-tolylphosphinous acid. The reaction takes place with the evolution of heat.

Table 2 lists various data about the esters of p-tolylmethylphosphinic acid.

TABLE 2

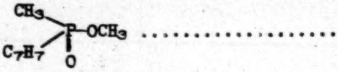
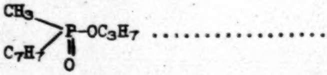
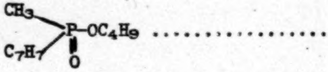
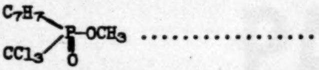
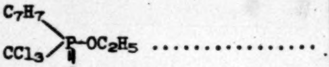
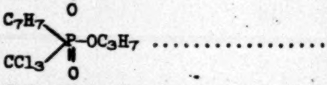
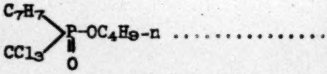
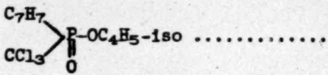
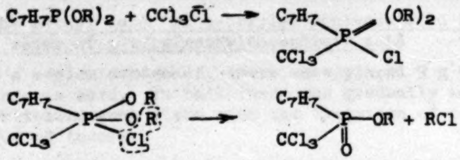
No. of comp.	Compound	Boiling point at 11-13 mm	d_0^0	n_D
1		151-152°	1.1315	1.5280
2		167	1.0830	1.5185
3		178	1.0722	1.5092

TABLE 3

No. of comp.	Compound	Boiling poing at 2 mm	d_0^0	n_D
1		128-130°	1.2328	1.5312
2		157-158	1.3260	1.5428
3		169-170	1.3094	1.5370
4		180-181	1.2303	1.5267
5		178-180	1.2661	1.5294

The esters of p-tolylmethylphosphinic acid are viscous colorless acid with weak odors. Upon heating with concentrated hydrochloric acid, they are saponified with the formation of p-tolylmethylphosphinic acid. This has m.p. 119-120°, and is identical with the compound previously investigated by Michaelis [3].

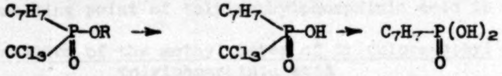
We next investigated the action of carbon tetrachloride on the esters of p-tolylphosphinous acid. This investigation showed that the esters of p-tolylphosphinous acid react easily, with the evolution of heat, with carbon tetrachloride, according to the following scheme:



By means of these experiments which are described in the experimental section of this report, we synthesized the esters listed in Table 3.

These esters which we obtained were colorless liquids with characteristic pleasant odors, and distilled without decomposition under high pressure.

The alkylated esters of trichloromethyl-p-tolylphosphinic acid, upon heating with hydrochloric acid, were saponified, in the first stage, with the elimination of alkyl chloride, to give trichloromethyl-p-tolylphosphinic acid. However, we must note that upon further heating, the trichloromethyl-p-tolylphosphinic acid, apparently, was hydrolyzed much more profoundly to give p-tolylphosphinic acid, according to the following scheme:



Later on, we shall continue with a more detailed investigation of the products of hydrolysis.

EXPERIMENTAL

The starting product, p-tolyldichlorophosphine, was obtained by the method of Michaelis and Paneck [2]. It was a colorless liquid with an unpleasant odor. B.p. 120° at 13 mm: d_8 1.2864; d_D^{20} 1.2666; n_D^{20} 1.5886.

The preparation of the methyl ester of p-tolylphosphinous acid

In a round-bottomed flask, fitted with a mechanical stirrer, a dropping funnel, and a reflux condenser, were placed 13.5 g of methyl alcohol, 50.2 g of dimethylaniline, and 100 ml of absolute ethyl ether. To this mixture there was added, with good cooling and continuous energetic stirring by means of the dropping funnel, 40 g of p-tolyldichlorophosphine. The reaction takes place with the evolution of a large amount of heat.

After the addition of the entire quantity of p-tolyldichlorophosphine, the contents of the flask were boiled on the water bath for 30 minutes. The next day the precipitated crystals of dimethylaniline hydrochloride were filtered off and washed with dry ether. The ether was then driven off on the water bath, and the residue distilled in vacuum.

The boiling point of the main fraction was 107-109° at 14 mm. Yield 52% of theory.

0.1017 g substance: 31.1 ml NaOH (1 ml NaOH = 0.5479 mg P).
Found %: P 16.77.
$C_9H_{13}O_2P$. Computed %: P 16.85.

The methyl ester of p-tolylphosphinous acid was a colorless mobile liquid, with an unpleasant, persistent odor. It reacted with copper monohalides:

d_8 1.0709; d_0^{10} 1.0427; n_D^{10} 1.5325.

The isomerization of the methyl ester of p-tolylphosphinous acid to give the methyl ester of p-tolylmethylphosphinic acid

In a flask fitted with a reflux condenser, there were placed 9 g of the methyl ester of p-tolylphosphinous acid. To this there was gradually added 5 g of methyl iodide. The isomerization took place with the evolution of considerable heat. The yield was about 90% of theory.

B.p. 151-152° at 13 mm.

0.1315 g substance: 40.05 ml NaOH (1 ml NaOH = 0.5479 mg P).
Found %: P 16.67.
$C_9H_{13}O_2P$. Computed %: P 16.85.

The ester obtained was a colorless liquid: d_0^0 1.1315; d_0^{15} 1.1204; n_D^{15} 1.5280.

The saponification of the methyl ester of p-tolylmethylphosphinic acid

5 g of the methyl ester of p-tolylmethylphosphinic acid and 15 ml of concentrated hydrochloric acid were boiled in a flask with a reflux condenser for 3 hours. After the hydrochloric acid had been removed, a crystalline substance was obtained. This was recrystallized from alcohol; m.p. 119-120°. According to Michaelis [3], the melting point of tolylmethylphosphinic acid is 120°.

The preparation of the methyl ester of trichloromethyl-p-tolylphosphinic acid

In a flask with a reflux condenser there were placed 9.5 g of carbon tetrachloride. To this there was gradually added 12 g of the methyl ester of p-tolylphosphinous acid. The reaction took place with unusual violence and the evolution of heat. During this reaction, methyl chloride separated out quantitatively. The remaining liquid was distilled in vacuum.

B.p. 128-130° at 1 mm; d_0^0 1.2328; d_0^{20} 1.2140; n_D^{20} 1.5312.

0.1238 g substance: 23.6 ml NaOH (1 ml NaOH = 0.5459 mg P).
Found %: P 10.41.
$C_8H_{10}O_2Cl_3P$. Computed %: P 10.77.

The methyl ester of trichloromethyl-p-tolylphosphinic acid is soluble in many organic solvents.

The preparation of the ethyl ester of p-tolylphosphinous acid

Using the above method 18.1 g of absolute ethyl alcohol, 50 g of dimethylaniline, and 40 g of p-tolyldichlorophosphine in absolute ethyl alcohol, 50 g of dimethylaniline, and 40 g of p-tolyldichlorophosphine in absolute ether were made to react to give the ethyl ester of p-tolylphosphinous acid. The boiling point of the main fraction was 123-125° at 9 mm. The yield was 19 g, or 50% of the theoretical.

0.1301 g substance: 35.4 ml NaOH (1 ml NaOH = 0.5459 mg P).
Found %: P 14.85.
$C_{11}H_{17}O_2P$. Computed %: P 14.63.

The ethyl ester of p-tolylphosphinous acid was a colorless mobile liquid with an unpleasant odor: d_0^{10} 1.0380; d_0^{18} 1.0210; n_D^{18} 1.5138

The isomerization of the ethyl ester of p-tolylphosphinous acid to give the ethyl ester of p-tolylethylphosphinic acid

In a flask fitted with a reflux condenser there were placed 9 g of the ethyl ester of p-tolylphosphinous acid and 6 g of ethyl iodide. The contents of the flask were boiled on the water bath for 2 hours. The boiling point of the isomerized product was 160° at 13 mm.

0.1316 g substance: 35.8 ml NaOH (1 ml NaOH = 0.5459 mg P)
Found %: P 14.85.
$C_{11}H_{17}O_2P$. Computed %: P 14.63.

The ethyl ester of ethyl-p-tolylphosphinic acid was a mobile, colorless liquid: d_0^0 1.0830; d_0^{18} 1.0697; n_D^{18} 1.5195.

The preparation of the ethyl ester of trichloromethyl-p-tolylphosphinic acid.

11 g of the ethyl ester of p-tolylphosphinous acid was placed in a flask. By means of a dropping funnel, 8 g of carbon tetrachloride was added in small portions. The reaction took place with the evolution of considerable heat. The reaction mixture was boiled on the water bath for 2 hours. After the boiling, the liquid had a yellowish color. The boiling point of the chief fraction was 157° at 2 mm.

0.1265 g substance: 0.1779 g AgCl.
0.1166 g substance: 22.7 ml NaOH (1 ml NaOH = 0.5459 mg P).
0.1288 g substance: 24.75 ml NaOH.
Found %: P 10.62, 10.49; Cl 34.79.
$C_{10}H_{12}O_2Cl_3P$. Computed %: P 10.38; Cl 35.20.

The ethyl ester of trichloromethyl-p-tolylphosphinic acid was a colorless oily liquid with a pleasant odor: d_0^0 1.3260; d_0^{18} 1.3103; n_D^{18} 1.5428.

The saponification of the ethyl ester of trichloromethyl-p-tolylphosphinic acid

4 g of the ethyl ester of trichloromethyl-p-tolylphosphinic acid and 12 ml of concentrated hydrochloric acid were boiled in a flask with a reflux condenser for 2 hours. After the hydrochloric acid had been removed by repeated evaporation with water on the water bath, a crystalline substance was obtained. The crystals were soluble in alcohol and in ether. After recrystallization from ether, they had m.p. 184.5-185°.

0.0922 g substance: 19.5 ml NaOH (1 ml NaOH = 0.5459 mg P).
0.0990 g substance: 21.1 ml NaOH.
0.1056 g substance: 0.1638 g AgCl.
Found %: P 11.54, 11.63; Cl 38.41.
$C_8H_8O_2Cl_3P$. Computed %: P 11.35; Cl 38.90.

The preparation of the n-propyl ester of p-tolylphosphinous acid

The n-propyl ester of p-tolylphosphinous acid was synthesized from 24 g of propyl alcohol, 50 g of dimethylaniline, and 40 g of p-tolyldichlorophosphine. The boiling point of the main fraction was 129-130° at 6 mm. The yield was 81.9% of theory. The ester was a colorless liquid:

0.1108 g substance: 24.8 mg NaOH (1 ml NaOH = 0.5718 mg P).
Found %: P 12.76.
$C_{13}H_{21}O_2P$. Computed %: P 12.92.

d_0^0 1.0091; d_0^{18} 0.9937; n_D^{18} 1.5070.

The action of methyl iodide on the propyl ester of p-tolylphosphinous acid

15 g of the propyl ester of p-tolylphosphinous acid were placed in a round-bottomed flask with a reflux condenser. 8.8 g of methyl iodide were added in small portions through a dropping funnel. The reaction took place with the evolution of considerable heat. To complete the reaction, the mixture was boiled on the water bath for 3 hours. The boiling point of the main fraction was 167° at 12 mm.

Yield 92% of theory.

0.1101 g substance: 28.7 ml NaOH (1 ml NaOH = 0.5718 mg P).
Found %: P 14.91.
$C_{11}H_{17}O_2P$. Computed %: P 14.62.

The propyl ester of methyl-p-tolylphosphinic acid was a colorless, mobile liquid, very soluble in ether, chloroform, and benzene: d_0^0 1.0889; d_0^{18} 1.0650; n_D^{18} 1.5185.

When the propyl ester of methyl-p-tolylphosphinic acid was saponified with hydrochloric acid, methyl-p-tolylphosphinic acid was obtained with m.p. 119-120°.

The preparation of the propyl ester of trichloromethyl-p-tolylphosphinic acid

15 g of the propyl ester of p-tolylphosphinous acid and 10 g of carbon tetrachloride gave the propyl ester of trichloromethyl-p-tolylphosphinic acid. B.p. 169-170° at 3 mm. Yield 12 g.

0.1194 g substance: 21.5 ml NaOH (1 ml NaOH = 0.5718 mg P).
Found %: P 10.27.
$C_{11}H_{14}O_2Cl_3P$. Computed %: P 9.84.

The propyl ester of trichloromethyl-p-tolylphosphinic acid was a colorless liquid with a pleasant odor. It was soluble in organic solvents: d_0^0 1.3094; d_0^{18} 1.2944; n_D^{18} 1.5370.

Upon saponification of the ester with hydrochloric acid, trichloromethyl-p-tolylphosphinic acid was obtained with m.p. 184°.

The preparation of the n-butyl ester of p-tolylphosphinous acid

The n-butyl ester of p-tolylphosphinous acid was synthesized from 30.7 g of butyl alcohol, 50 g of dimethylaniline, and 40 g of p-tolyldichlorophosphine in absolute ether. B.p. 170-171° at 13 mm. Yield 89.3% of theory.

0.1168 g substance: 24.8 ml NaOH (1 ml NaOH = 0.5519 mg P).
0.1228 g substance: 25.4 ml NaOH.
Found %: P 11.75, 11.42.
$C_{15}H_{25}O_2P$. Computed %: P 11.57.

This ester was a colorless liquid with an unpleasant odor, insoluble in water, easily soluble in ether and in alcohol: d_0^0 0.9899; d_0^{18} 0.9776; n_D^{18} 1.5024.

The action of methyl iodide on the n-butyl ester of p-tolylphosphinous acid

The action of 5.2 g of methyl iodide on 10 g of the n-butyl ester of p-tolylphosphinous acid gave the n-butyl ester of methyl-p-tolylphosphinic acid. This compound was a colorless liquid. Its b.p. was 178° at 11 mm. Yield 7.6 g, or about 90% of theory. d_0^0 1.0722; d_0^{18} 1.0583; n_D^{18} 1.5092.

0.1124 g substance: 27.6 ml NaOH (1 ml NaOH = 0.5519 mg P).
0.1160 g substance: 28.3 ml NaOH.
Found %: P 13.55, 13.51.
$C_{12}H_{19}O_2P$. Computed %: P 13.72.

Saponification of the butyl ester of methyl-p-tolylphosphinic acid with hydrochloric acid under the influence of heat gave methyl-p-tolylphosphinic acid with m.p. 119-120°.

The preparation of the butyl ester of trichloromethyl-p-tolylphosphinic acid

The preparation of this ester was carried by a similar method, i.e., by heating 10 g of the butyl ester of p-tolylphosphinous acid and 5.7 g of carbon tetrachloride under the same conditions. After the butyl chloride had been driven off, the viscous liquid which remained was distilled under vacuum. The ester obtained was a colorless liquid.

B.p. 180-181° at 2 mm: d_0^8 1.2303; d_0^{16} 1.2143; n_D^{16} 1.5267.

0.1003 g substance: 0.1289 g AgCl.
0.1042 g substance: 18.4 ml NaOH (1 ml NaOH = 0.5519 mg P).
0.1078 g substance: (19.1 ml NaOH (1 ml NaOH = 0.55 k/mg.)
Found %: P 9.74, 9.77; Cl 32.28.
$C_{12}H_{16}O_2Cl_3P$. Computed %: P 19.42; Cl 31.79.

Saponificatinn of the ester gave p-tolyltrichloromethylphosphinic acid, with m.p. 184°.

The preparation of the isobutyl ester of trichloromethyl-p-tolylphosphinous acid

The isobutyl ester of p-tolylphosphinous acid was synthesized from 30.7 g of isobutyl alcohol, 50 g of dimethylaniline, and 40 g of p-tolyldichlorophosphine.

B.p. 155-156° at 13 mm. Yield 44 g, or about 77% of theory.

0.1075 g substance: 22.8 ml NaOH.
0.1051 g substance: 22.4 ml NaOH (1 ml NaOH = 0.5519 mg P).
Found %: P 11.70, 11.76.
$C_{15}H_{25}O_2P$. Computed %: P 11.57.

The isobutyl ester of p-tolylphosphinous acid was a colorless, mobile liquid with a slightly unpleasant odor: d_0^8 0.9807; d_0^{16} 0.9667; n_D^{16} 1.4987.

The preparation of the isobutyl ester of trichloromethyl-p-tolylphosphinic acid

The isobutyl ester of trichloromethyl-p-tolylphosphinic acid was prepared from 16 g of the isobutyl ester of p-tolylphosphinous acid and 9.2 g of carbon tetrachloride. The reaction took place with the evolution of considerable heat. Isobutyl chloride was given off almost quantitatively. The yield of ester was about 58% of theory. The ester was a transparent liquid with a pleasant odor. d_0^8 1.2661; d_0^{16} 1.2250; n_D^{16} 1.5294.

B.p. 178-180° at 4 mm.
0.1368 g substance: 23.8 ml NaOH (1 ml NaOH = 0.5519 mg P).
Found %: P 9.60.
$C_{12}H_{16}O_2Cl_3P$. Computed % P 9.42.

Upon heating with hydrochloric acid, the isobutyl ester of trichloromethyl-p-tolylphosphinic acid was saponified to give the trichloromethyl-p-tolylphosphinic acid, with m.p. 184°.

SUMMARY

1. The reaction of p-tolyldichlorophosphine with various alcohols in the presence of dimethylaniline gave new representatives of the esters of p-tolylphosphinous acid. These were investigated.

2. The esters of p-tolylphosphinous acid, as derivatives of trivalent phosphorus, reacted with copper monohalides, methyl iodide and carbon tetrachloride.

3. Various esters of p-tolylmethylphosphinic acid have been synthesized and studied.

4. The action of carbon tetrachloride on various esters of p-tolylphosphinous acid permitted the synthesis and study of the corresponding esters of trichloromethyl-p-tolylphosphinic acid.

5. The saponification of esters of trichloromethyl-p-tolylphosphinic acid by means of hydrochloric acid gave trichloromethyl-p-tolylphosphinic acid in crystalline form.

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[3] Michaelis Ber., 31, 1046 (1898).

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THE SYNTHESIS AND TRANSFORMATION OF

β-(1-ALKOXYTETRAHYDRONAPHTHOYL-4) PROPIONIC ACIDS

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In a preceding paper [1] we have reported the synthesis and proved the structure of β-(1-ethoxytetrahydronaphthoyl-4)-propionic acid. The objective of the present work was to prepare β-(1-alkoxytetrahydronaphthoyl-4)-propionic acids with high alkyl radicals in the ether group.

Several of these keto acids (propoxy, butoxy, and heptoxy- tetrahydronaphthoylpropionic acids) have been obtained by us by condensing the corresponding alkyl ethers of ar-α-tetralol with succinic anhydride in the presence of $AlCl_3$. During these reactions, it was observed that an increase in size of the alkyl radical considerably lowered the yield of keto acid, as the reactions are accompanied by considerable tarring, and this complicates the isolation and purification of the keto acids (in these cases it was necessary to subject to esterification the oily product obtained directly after carrying out the reaction, to purify the ester, and then to saponify it).

These difficulties forced us to seek for another means of obtaining the higher 1-alkoxytetrahydronaphthoyl-4-propionic acids.

It appeared to us that the simplest thing would be to obtain 1-hydroxytetrahydronaphthoyl-4-propionic acid some how or other, and then to alkylate the hydroxyl group in this.

As the experiments on the condensation of ar-α-tetralol with succinic anhydride did not result in the isolation of 1-hydroxytetrahydronaphthoyl-4-propionic acid, we investigated the reaction in which the ether groups are split off from the easily obtainable 1-methoxy- [2] and 1-ethoxy- tetrahydronaphthoyl-4-propionic acids. We found that when these acids were heated with $AlCl_3$ in benzene solution (this method has been applied successfully for similar compounds of the naphthalene series), 1-hydroxytetrahydronaphthoyl-4-propionic acid could be easily obtained in sufficient quantity, whereas the more widely used method of hydrolysis by means of hydrobromic acid in this case appeared unfavorable. To alkylate the 1-hydroxytetrahydronaphthoyl-4-propionic acid, we used the corresponding alkyl halide, and thus obtained the 1-hexoxy- and 1-heptoxy- tetrahydronaphthoyl-4-propionic acids.

The transition from the lower 1-alkoxytetrahydronaphthoyl-4-propionic acids to the higher members is shown by the following scheme:

$$ROC_{10}H_{10}CO(CH_2)_2COOH \xrightarrow[C_6H_6]{AlCl_3} HOC_{10}H_{10}CO(CH_2)_2COOH \xrightarrow[H_2SO_4]{C_2H_5OH}$$

$$\longrightarrow HOC_{10}H_{10}CO(CH_2)_2COOC_2H_5 \xrightarrow{R_1X} R_1OC_{10}H_{10}CO(CH_2)_2COOC_2H_5 \xrightarrow[C_2H_5OH]{KOH}$$

$$\longrightarrow R_1OC_{10}H_{10}CO(CH_2)_2COOH. \quad (R = CH_3,\ C_2H_5.\ R_1 = C_6H_{13},\ C_7H_{15}).$$

This method of cleaving the ether group can be applied to any alkoxyketo acid of this series, and made it possible for us to confirm experimentally the structure of 1-butoxytetrahydronaphthoyl-4-propionic acid which we had assumed on the basis of analogy, as the dealkylization of this acid gave 1-hydroxytetrahydronaphthoyl-4-propionic acid.

By means of the Clemmensen reaction, we obtained from 1-butoxy- and 1-hydroxy 4-tetrahydronaphthoylpropionic acid 1-butoxy- and 1-hydroxy-4-naphthylbutyric acids.

EXPERIMENTAL

1. 1-Methoxytetralin *

74 g of α-tetralol was dissolved in an alcoholic solution of KOH (31 g of KOH in 125 ml of absolute alcohol). To this solution, 177 g of methyliodide in 25 ml of absolute alcohol were added, and the mixture heated for 3 hours. After the usual treatment, the substance obtained was distilled in vacuum. The boiling point of the 1-methoxytetraline was 129-131° at 19 mm. Yield 62 g.

3.010 mg substance: 8.972 mg CO_2; 2.930 mg H_2O.
Found %: C 81.29; H 8.66.
$C_{11}H_{14}O$. Computed %: C 81.48; H 8.64.

The methyl ester of β-(1-methoxy-5,6,7,8-tetrahydronaphthoyl-4-)-propionic acid

50 ml of absolute methyl alcohol and 1 ml of concentrated sulfuric acid were added to 5 g of β-(1-methoxytetrahydronaphthoyl-4)-propionic acid with m.p. 177-179°** (obtained by the condensation of 1-methoxytetralin with succinic anhydride). The mixture was heated for 6 hours. The usual treatment gave 4 g of material. Recrystallization from a mixture of acetone and alcohol gave faintly colored crystals with m.p. 80-82.5°. The methyl ester of β-1-methoxytetrahydronaphthoyl-4)-propionic acid was very easily soluble in benzene, chloroform, and acetone, soluble with more difficulty in alcohol, and insoluble in water.

3.466 mg substance: 8.850 mg CO_2; 2.292 mg H_2O.
3.010 mg substance: 7.665 mg CO_2; 1.981 mg H_2O.
Found %: C 69.64, 69.45; H 7.40, 7.36.
$C_{16}H_{20}O_4$. Computed %: C 69.56; H 7.24.

Saponification of a sample of the ester with alcoholic caustic potash gave β-(1-methoxytetrahydronaphthoyl-4)-propionic acid, with m.p. 176-178°. After recrystallization from alcohol, the m.p. was 177-179°.

2. 1-Propoxytetralin

31 g of caustic potash was heated with 125 ml of absolute alcohol until as much as possible of the caustic potash had dissolved, and 74 g of α-tetralol was then added. The resulting solution was heated, and to it was gradually added 170 g of propyl bromide in 125 ml of absolute alcohol. Heating was continued for 2 to 3 hours. The alcohol was driven off, and water added to the residue. This was extracted with ether, and the ether extract was washed with 1 N alkali, then with water, and dried over calcium chloride. The ether was driven off. The residue was distilled in vacuum. 70 g of 1-propoxytetralin was obtained. This was a mobile liquid with b.p. 141-142° at 16-17 mm.

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*1-Methoxytetralin has also been obtained by Bachmann and Ness (loc.cit.) from α-tetralol and methyl sulfate.

**Bachmann and Ness (loc. cit.) give the m.p. of 1-methoxytetrahydronaphthoyl-4-propionic acid as 176-177°.

3.970 mg substance: 11.940 mg CO_2; 3.339 mg H_2O.
Found %: C 82.03; H 9.42.
$C_{13}H_{18}O$. Computed %: C 82.10; H 9.47.

β-(1-Propoxy-5,6,7,8-tetrahydronaphthoyl-4-)-propionic acid and its methyl ester

a) The condensation of 1-propoxy-5,6,7,8-tetrahydronaphthalene with succinic anhydride. To 30 g of 1-propoxytetralin, 16 g of succinic anhydride in 400 ml of dry nitrobenzene was added gradually at room temperature, and then, with mechanical stirring 48 g of aluminum chloride was added. The reaction mixture was allowed to stand until the following day, and stirring again continued for 6 hours. The mixture was then decomposed with ice water in the presence of hydrochloric acid. The nitrobenzene layer was separated from the aqueous. Ether was added to the nitrobenzene solution, and the resulting solution was shaken with a 4% solution of alkali. The traces of ether were removed from the alkaline layer by heating and the latter was filtered. Acidification of the alkaline solution gave a tar, which was dried for several days in the vacuum dessicator. After this, it hardened sufficiently to be converted into a powder. 32 g of the unpurified keto acid was obtained. Purification of the acid was carried out by preparation of its ester and saponification of the latter.

b) The methyl ester of β-(1-propoxy-5,6,7,8-tetrahydronaphthoyl-4)-propionic acid. To 43 g of the unpurified keto acid thus obtained, there was added 400 ml of absolute methyl alcohol and 6 ml of concentrated sulfuric acid. The mixture was heated on the water bath for 6 hours. The alcohol was driven off. The residue was diluted with water and extracted with ether. The ether extract was washed with a 3% solution of sodium bicarbonate, and then with water. It was dried over anhydrous sodium sulfate. The ether was driven off to leave an oil, which distilled at 216-222° at 4-5 mm. Upon cooling, the oil crystallized. 21 g was obtained; recrystallization from alcohol gave 15 g of the methyl ester of 1-propoxytetrahydronaphthoyl-4-propionic acid with m.p. 39-41°. Part of this substance was recrystallized again. After two recrystallizations from alcohol (the first with the addition of charcoal) the m.p. was 47-48°. The substance was colorless and crystalline, easily soluble without heating in benzene, chloroform, and acetone, soluble with more difficulty in alcohol, and insoluble in water.

3.621 mg substance: 9.391 mg CO_2; 2.579 mg H_2O.
4.238 mg substance: 10.988 mg CO_2; 2.983 mg H_2O.
Found %: C 70.73, 70.71; H 7.97, 7.88.
$C_{18}H_{24}O_4$. Computed %: C 71.05; H 7.89.

c) β-(1-Propoxy-5,6,7,8-tetrahydronaphthoyl-4)-propionic acid, – $C_3H_7OC_{10}H_{10}CO(CH_2)_2COOH$. To 1.2 g of the methyl ester of 1-propoxytetrahydronaphthoyl-4-propionic acid with m.p. 47-48° there were added 12 ml of alcohol and 0.8 g of KOH. The solution was heated over a water bath for 6 hours. The alcohol was driven off. The residue was taken up in water and acidified with 10% hydrochloric acid. A precipitate formed and was filtered off, and washed several times with water. 0.9 g of a material with m.p. 131-134° was obtained. Recrystallization from alcohol gave a faintly colored crystalline material with m.p. 134-137°. 1-Propoxytetrahydronaphthoyl-4-propionic acid was very soluble in chloroform, acetone, benzene, and alcohol, slightly soluble in hot water.

3.639 mg substance: 9.370 mg CO_2; 2.520 mg H_2O.
3.490 mg substance: 8.972 mg CO_2; 2.369 mg H_2O.
Found %: C 70.22, 70.11; H 7.74, 7.60.
$C_{17}H_{22}O_4$. Computed %: C 70.34; H 7.58.

In order to obtain 1-propoxytetrahydronaphthoyl-4-propionic acid we can also use the methyl ester of 1-propoxytetrahydronaphthoyl-4-propionic acid, which has a lower melting point.

We used 14.6 g of the methyl ester of 1-propoxytetrahydronaphthoylpropionic acid with m.p. 39-41°, 9.5 g of KOH, and 150 ml of alcohol. After two recrystallizations from alcohol, 8 g of the keto acid with m.p. 134-137° was obtained.

3. 1-Butoxytetralin

This was obtained by the same method as was used for propoxytetralin. For the reaction, 40 g of α-tetralol, 16.5 g of KOH in 70 ml of absolute alcohol and 55 g of butyl bromide in 55 ml of absolute alcohol were used. After the usual treatment, the substance obtained was distilled in vacuum; 42 g of the fraction boiling at 133-150° at 14-15 mm was collected. This material was dissolved in ether and washed with Claisen's mixture. After the ether had been driven off, a vacuum distillation gave 35 g of 1-butoxytetralin with b.p. 168-170° at 22 mm.

3.077 mg substance: 9.299 mg CO_2; 2.697 mg H_2O.
3.722 mg substance: 11.218 mg CO_2; 3.250 mg H_2O.
Found %: C 82.42, 82.20; H 9.81, 9.77.
$C_{14}H_{20}O$. Computed %: C 83.25; H 9,80.

β-(1-Butoxy-5,6,7,8-tetrahydronaphthoyl-4)-propionic acid and its methyl ester

a) The condensation of 1-butoxy-5,6,7,8-tetrahydronaphthalene with succinic anhydride. 12 g of succinic anhydride and 300 ml of dry nitrobenzene were added to 22 g of 1-butoxytetralin. After some stirring, there was gradually added, with additional mechanical stirring, 36 g of aluminum chloride. The reaction took place at room temperature. The mixture was allowed to stand until the following day and stirring was again continued for 5 or 6 hours. At the end of the reaction, the mixture was decomposed with water containing ice and hydrochloric acid. The nitrobenzene layer was separated from the aqueous, and ether added to the nitrobenzene layer. The ethereal solution was then extracted with a 4% solution of alkali. Traces of ether were driven off from the alkaline layer by heating. It was then filtered and the alkaline solution acidified with 10% hydrochloric acid. The keto acid precipitated in the form of a tar, which was dried on the water bath. 25 g of the unpurified keto acid was obtained. The purification of the acid was carried out by preparing its ester and saponifying the latter.

b) The methyl ester of 1-butoxy-5,6,7,8-tetrahydronaphthoyl-4-propionic acid. This was obtained by the same method as the methyl ester of propoxytetrahydronaphthoyl-4-propionic acid.

30 g of the unpurified keto acid gave 11 g of material in the form of an oil, which was distilled at 228-232° at 5-6 mm. This crystallized upon rubbing Recrystallization from alcohol gave 6 g of a substance with m.p. 28-32°. A second recrystallization from alcohol raised the m.p. to 35-36°. The methyl ester of 1-butoxytetrahydronaphthoyl-4-propionic acid was a crystalline substance in the form of small needles. It dissolved easily in organic solvents, and was insoluble in water.

4.190 mg substance: 10,998 mg CO_2; 3.011 mg H_2O.
2.859 mg substance: 7.482 mg CO_2; 2.028 mg H_2O.
Found %: C 71.59, 71.37; H 8.04, 7.94.
$C_{19}H_{26}O_4$. Computed %: C 71.70; H 8.14.

c) β-(1-Butoxy-5,6,7,8-tetrahydronaphthoyl-4)-propionic acid $C_4H_9OC_{10}H_{10}CO(CH_2)_2COOH$. Saponification of 16 g of the methyl ester of butoxytetrahydronaphthoyl-4-propionic acid with m.p. 28-32° with alcoholic alkali (9.5 g of KOH and 160 ml of alcohol) gave 15 g of the keto acid with m.p. 111-113°. A recrystallization from alcohol gave a crystalline substance with m.p. 114-117°. 1-Butoxytetrahydronaphthoyl-4-propionic acid was very soluble in organic solvents.

3.773 mg substance: 9.809 mg CO_2; 2.610 mg H_2O.
3.236 mg substance: 8.418 mg CO_2; 2.270 mg H_2O.
Found %: C 70.90, 70.95; H 7.74, 7.85.
$C_{18}H_{24}O_4$. Computed %: C 71.05; H 7.89.

β-(1-Butoxy-5,6,7,8-tetrahydronaphthyl-4)-butyric acid $C_4H_9OC_{10}H_{10}(CH_2)_3COOH$

To 5 g of 1-butoxytetrahydronaphthoyl-4-propionic acid there were added 33 ml of hydrochloric acid (1:1), 33 ml of glacial acetic acid, 33 ml of toluene, and 25 g of amalgamated zinc. The reaction was carried out with heating for 21 hours. 3 ml portions of hydrochloric acid (1:1) were added 3 times during the reaction. At the end of the reaction, the contents of the flask were extracted with ether. The acid which had formed was extracted from the ether layer with a 4% solution of KOH. The alkaline solution was heated to remove traces of ether, and acidified with 10% hydrochloric acid. It was recrystallized once from alcohol, and then from aqueous methyl alcohol. 2.7 g of 1-butoxy-5,6,7,8-tetrahydronaphthoylbutyric acid was obtained, with m.p. 90-92°.

5.036 mg substance: 13.725 mg CO_2; 4.020 mg H_2O.
Found %: C 74.33; H 8.93.
$C_{18}H_{28}O_3$. Computed %: C 74.48; H 8.96.

4. 1-Heptoxytetralin

This was obtained by the same method described above for the preparation of alkoxy tetralins. For the reaction, 14.8 g of α-tetralin, 6.2 g of KOH in 25 ml of absolute alcohol, and 25 g of heptyl bromide in 25 ml of absolute alcohol were used. The heating was continued for 2 hours.

After the proper treatment, 14 g of 1-heptoxytetralin with b.p. 178-180° at 11-12 mm were obtained.

4.749 mg substance: 14.476 mg CO_2; 4.458 mg H_2O.
Found %: C 83.13; H 10.50.
$C_{17}H_{28}O$. Computed %: C 82.92; H 10.57.

β-(1-Heptoxy-5 6,7,8-tetrahydronaphthoyl-4)-propionic acid and its methyl and ethyl esters

1. The preparation of 1-heptoxy-5,6,7,8-tetrahydronaphthoyl-4-propionic acid by the condensation of 1-heptoxytetrahydrotetralin with succinic anhydride

4.1 g of succinic anhydride in 140 ml of dry nitrobenzene was added to 10 g of 1-heptoxytetralin. Then there was gradually added, with mechanical stirring, 16.5 g of aluminum chloride. The reaction took place at room temperature. It was allowed to stand until the following day and stirring again continued for 5-6 hours. At the end of the reaction, the mixture was decomposed with water containing ice and hydrochloric acid. The nitrobenzene layer was separated from the aqueous.* The nitrobenzene was driven off with steam. In the distillation flask there remained 10 g of a tarry residue. The acid was isolated and purified by esterification and subsequent saponification of the ester.

The methyl ester of 1-heptoxy-5,6,7,8-tetrahydronaphthoyl-4-propionic acid was obtained by the method indicated above for the preparation of esters of 1-alkoxytetrahydronaphthoyl-4-propionic acid. 10 g of the unpurified 1-heptoxytetrahydronaphthoyl-4-propionic acid gave 6 g of an oily substance with b.p. 215-220° at 5-6 mm.

In this case we did not extract the 1-heptoxytetrahydronaphthoyl-4-propionic acid from the nitrobenzene solution with alkali as the sodium salt of 1-heptoxytetrahydronaphthoyl-4-propionic acid is soluble with difficulty in water.

6 g of this methyl ester was saponified with aqueous-alcoholic alkali (2.5 g of KOH and 50 ml of alcohol). 3 g of the unpurified 1-heptoxytetrahydronaphthoyl-4-propionic acid was obtained. After 2 recrystallizations from alcohol, its m.p. was 91-92°.

4.879 mg substance: 13.086 mg CO_2; 3.828 mg H_2O.
Found %: C 73.15; H 8.77.
$C_{21}H_{30}O_4$. Computed %: C 72.83; H 8.67.

II. The preparation of 1-heptoxy-5,6,7,8-tetrahydronaphthoyl-4-propionic acid by the alkylation of the ethyl ester of 1-hydroxytetrahydronaphthoyl-4-propionic acid

a) The ethyl ester of β-(1-heptoxy-5,6,7,8-tetrahydronaphthoyl-4)-propionic acid. 2.3 g of caustic potash was dissolved in 30 ml of absolute alcohol and to the solution there was added 10 g of the ethyl ester of 1-hydroxytetrahydronaphthoyl-4-propionic acid. Then, while the solution was heated, there was added gradually 15 g of heptyl bromide, dissolved in 20 ml of absolute alcohol. After the heptyl bromide had all been added, heating was continued for 2 hours.

The potassium bromide was filtered off and the alcohol evaporated. The residue was diluted with water, extracted with ether, and the ether extract dried over sodium sulfate. After the ether had been driven off and the unreacted heptyl bromide along with it, the residue distilled at 215-218° at 3-4 mm. Yield 10 g.

The ethyl ester of β-(heptoxytetrahydronaphthoyl-4)-propionic acid was obtained with the same boiling point by the esterification of 1-heptoxytetrahydronaphthoyl-4-propionic acid.

b) β-(1-Heptoxy-5,6,7,8-tetrahydronaphthoyl-4)-propionic acid, $C_7H_{15}OC_{10}H_{10}CO(CH_2)_2COOH$. 4.2 g of caustic potash were heated with 70 ml of alcohol. To the alcoholic alkali solution there were added 9 g of the ethyl ester of 1-heptoxy-5,6,7,8-tetrahydronaphthoyl-4-propionic acid (cf. preceding experiment) and the solution was heated for 6 hours. The alcohol was driven off. Water was added to the residue, which was then solidified with 10% hydrochloric acid. The precipitate of keto acid was filtered off with suction, and washed with water. Recrystallization from alcohol gave 4 g of a crystalline substance with m.p. 90-92°.

3.685 mg substance: 9.845 mg CO_2; 2.745 mg H_2O.
Found %: C 72.86; H 8.54.
$C_{21}H_{30}O_4$. Computed %: C 72.83; H 8.67.

5. β-(1-Hexoxytetrahydronaphthoyl-4)-propionic acid and its ethyl ester

a) The ethyl ester of β-(1-hexoxytetrahydronaphthoyl-4)-propionic acid. 2.3 g of caustic alkali was heated with 30 ml of absolute alcohol, and 10 g of the ethyl ester of 1-hydroxytetrahydronaphthoylpropionic acid was then added. This solution was heated and 18 g of hexyl iodide, dissolved in 30 ml of absolute alcohol, was gradually added. After all the hexyl iodide had been added, heating was continued for 2 hours. The usual treatment gave an oily material which distilled over at 235-240° at 6-7 mm.

The same boiling point was obtained for the ethyl ester of β-1-hexoxytetrahydronaphthoyl-4-propionic acid obtained by esterifying 1-hexoxytetrahydronaphthoyl-4-propionic acid.

b) β-(Hexoxy-5,6,7,8-tetrahydronaphthoyl-4)-propionic acid, $C_6H_{13}OC_{10}H_{10}CO(CH_2)_2COOH$. 4 g of caustic potash was heated with 65 ml of alcohol. To the alcoholic-alkali solution there was added 8.5 g of the ethyl ester of 1-hexoxytetrahydronaphthoyl-4-propionic acid. The solution was heated for 6 hours.

The alcohol was driven off. The residue was diluted with water and acidified with 10% hydrochloric acid. The precipitated keto acid was filtered with suction and washed with water. Yield 4.5 g. 1-Hexoxytetrahydronaphthoyl-4-propionic acid was a crystalline compound, easily soluble in organic solvents. Recrystallization from alcohol, using charcoal, gave a melting point of 92-94°.

3.215 mg substance: 8.548 mg CO_2; 2.480 mg H_2O.
Found %: C 72.51; H 8.63.
$C_{20}H_{28}O_4$. Computed %: C 72.29; H 8.43.

6. 1-Hydroxytetrahydronaphthoyl-4-propionic acid, $HOC_{10}H_{10}CO(CH_2)_2COOH$, The preparation of 1-methoxy-, 1-ethoxy-, and 1-butoxy-tetrahydronaphthoyl-propionic acids by saponification

a) 6 g of 1-methoxytetrahydronaphthoyl-4-propionic acid was dissolved in 60 ml of glacial acetic acid and 20 ml of a 48% aqueous solution of HBr was added to the solution. The solution was heated on the oil bath at 120-130° for 4 hours. The acetic acid and HBr were driven off in vacuum until the residue was dry. To the residue, a 10% solution of alkali was added. The insoluble portion was filtered off. Upon acidification of the alkaline solution, 2 g of a precipitate formed. This was recrystallized from acetone and then from a mixture of benzene and alcohol. (The substance was first heated in benzene, and then, while the heating was continued, the alcohol was added drop by drop until solution was complete). Upon cooling, colorless crystals precipitated out, with m.p. 192-194.5°. 1 g of 1-hydroxytetrahydronaphthoyl-4-propionic acid was obtained. It was easily soluble without heating in acetone and alcohol, and soluble with difficulty in benzene and in hot water.

2.793 mg substance: 6.960 mg CO_2; 1.600 mg H_2O.
Found %: C 67.96; H 6.41.
$C_{14}H_{16}O_4$. Computed %: C 67.74; H 6.45.

b) 27 g of 1-methoxytetrahydronaphthoyl-4-propionic acid was dissolved with heating in 1160 ml of absolute benzene. This was then allowed to stand and 55 g of aluminum chloride was then added in several portions and heated for 5 hours. The benzene was driven off almost to dryness, and the residue decomposed with water containing ice and 120 ml of concentrated hydrochloric acid. The precipitate was filtered off and washed with water. It was then dissolved by heating in a 10% solution of alkali to which charcoal was added. The alkaline solution was filtered and acidified with 10% hydrochloric acid. The precipitate was filtered off and washed several times with water. 23 g of unpurified material was obtained with m.p. 174-182°. Recrystallization from hot water gave 14 g of material with m.p. 184-190°. Recrystallization from a mixture of benzene and alcohol gave 11.5 g of colorless crystals, with m.p. 192-194.5°.

c) 900 ml of dry benzene was added to 21 g of 1-ethoxytetrahydronaphthoyl-4-propionic acid and heated to boiling. The mixture was then allowed to stand and 42 g of aluminum chloride was added in several portions. The reaction mixture was heated for 4 or 5 hours. The benzene was driven off, and the product of reaction was decomposed with water containing ice and concentrated hydrochloric acid. The precipitate obtained was dissolved in a 10% solution of alkali, and the alkaline solution acidified with 10% hydrochloric acid. The substance was recrystallized from hot water. 13 g were obtained, with m.p. 190-195°. After recrystallization from a mixture of benzene and alcohol, 9 g was obtained, with m.p. 192-195°.

d) 4 g of 1-butoxytetrahydronaphthoyl-4-propionic acid gave 1.2 g of

1-hydroxytetrahydronaphthoyl-4-propionic acid by the same method as has been described for the previous experiments on the saponification of the 1-methoxy- and 1-ethoxy- tetrahydronaphthoyl-4-propionic acids. A mixed test of this acid of m.p. 192-196° with the 1-hydroxytetrahydronaphthoyl-4-propionic acid obtained by the saponification of 1-methoxytetrahydronaphthoyl-4-propionic acid, of m.p. 192-195°, gave m.p. 192-195°.

The ethyl ester of 1-hydroxy-5,6,7,8-tetrahydronaphthoyl-4-propionic acid

45 ml of absolute alcohol and 2.5 ml of concentrated sulfuric acid were added to 4.5 g of 1-hydroxytetrahydronaphthoyl-4-propionic acid, and the mixture heated for 6 hours. The alcohol was driven off and the residue diluted with water. The precipitate was filtered off and washed with water. The precipitate was dissolved in ether, and the ethereal solution washed with a 3% solution of sodium bicarbonate and then with water. The ethereal extract was dried over anhydrous sodium sulfate. The ether was driven off and the residue recrystallized from methyl alcohol. 3 g of substance was obtained with m.p. 122-124°. The ethyl ester of 1-hydroxytetrahydronaphthoyl-4-propionic acid was in the form of colorless crystals, easily soluble in organic solvents, and insoluble in water.

3.039 mg substance: 7.735 mg CO_2; 1.990 mg H_2O.
Found %: C 69.41; H 7.32.
$C_{16}H_{20}O_4$. Computed %: C 69.56; H 7.24.

β-(1-hydroxy-5,6,7,8-tetrahydronaphthyl-4)-butyric acid, $HOC_{10}H_{10}(CH_2)_3COOH$

1-Hydroxytetrahydronaphthyl-4-butyric acid was obtained by means of a Clemmensen reduction of 1-hydroxytetrahydronaphthoyl-4-propionic acid. 2 g of the latter acid gave 1.3 g of product. After 2 recrystallizations from dichloroethane, the m.p. was 127-130°. The colorless crystals were easily soluble in organic solvents.

3.310 mg substance: 8.688 mg CO_2; 2.288 mg H_2O.
Found %: C 71.58; H 7.73.
$C_{14}H_{18}O_3$. Computed %: C 71.79; H 7.69.

SUMMARY

1. The condensation of esters of ar-α-tetralol with succinic anhydride gave 1-propoxy, 1-butoxy-, and 1-heptoxy-4-tetrahydronaphthoylpropionic acids.

2. The splitting off of ether groups from 1-alkoxy-4-tetrahydronaphthoylpropionic acids has been investigated. When keto acids of this type are heated with $AlCl_3$ in benzene solution, 1-hydroxy-4-tetrahydronaphthoylpropionic acid is readily formed.

3. By alkylating the ethyl ester of 1-hydroxy-4-tetrahydronaphthoylpropionic acid with alkyl halides and then hydrolyzing the ester group, 1-hexoxy and 1-heptoxy-4-tetrahydronaphthoylpropionic acids were obtained.

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MANGANESE TETRAACETATE AS AN OXIDIZING AGENT FOR ORGANIC COMPOUNDS

I. THE QUESTION OF THE OXIDATION OF α GLYCOLS

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Along with the well-known oxidizing agents, like potassium permanganate, potassium dichromate, chromic anhydride and others, there are references in the literature to less well-known oxidizing agents, like selenous anhydride [1], lead tetracetate [2], and iodic acid [3].

To the number of oxidizing agents of organic compounds, as the work of one of us has shown [4], we can add manganese triacetate. This oxidizing agent has a great selective power in oxidizing reactions.

There is no reference in the literature to the oxidative power of the acetate of tetravalent manganese. It appeared to us of interest to carry out a systematic investigation of the oxidizing power of this manganese acetate, in the first place, to study the influence of the valence of the manganese on the process of oxidation, and in the second place, to investigate the influence of the solvent and the structure of the compound on the speed and mechanism of the reaction.

We began our investigations with α-glycols.

According to the data of Griegee [2], the oxidation of α-glycols by lead tetracetate in different solvents takes place by means of the formation of a lead substituted glycol of the alcoholate type. This hypothetical mechanism of Griegee was confirmed by the different velocities of oxidation of cis and trans isomers of the glycols, and also by the various velocities of oxidation of glycols in different solvents. The velocity of the oxidation in a solution of acetic acid is much less than a thousandth of that in indifferent solvents like benzene, nitrobenzene, chloroform, and dichloroethane.

Griegee explained the comparative inertia of the reaction in acetic acid by the formation of an intermediate product with a cyclic structure — a lead glycolate, which, in the author's opinion, was stable in acetic acid.

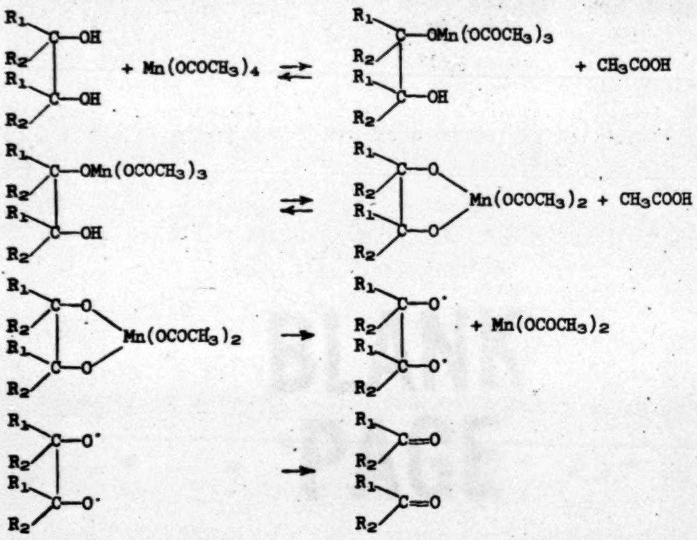
In his article on the oxidation of α-glycols, Griegee observes that the acetates of other metals with several valences behave in similar ways, but gives no experimental data.

Our investigations showed that manganese tetracetate is an oxidizing agent of organic compounds, and that the velocity of the oxidation in different solvents is different from that of lead tetracetate.

All the glycols we investigated, both of the aliphatic and aromatic series, were oxidized by manganese tetracetate, in contradistinction to the results with lead tetracetate, more quickly in acetic acid than in inert solvents.

We determined that manganese tetracetate, like manganese triacetate, oxidizes glycols to give carbonyl derivatives. The end-product of the oxidation of benzopinacone is benzophenone; of pinacone, acetone; of symm. dimethyldiphenylethylene glycol, acetophenone; of trimethylphenylethylene glycol, acetone and acetophenone; of hydrobenzoin, benzaldehyde.

This makes it possible to represent the oxidatinn of α-glycols, as was the case with $Mn(OCOCH_3)_3$, by means of intermediate stages of the formation of radicals according to the scheme:



The formation of carbonyl compounds is shown by the formation of oximes and by qualitative reactions.

Measurements of the velocity of oxidation of a list of glycols (Tables 2, 3, 4, and 5)* made it possible to determine various regularities shown in the relationships between reaction velocity and temperature, structure of compound, and solvent.

From these tables, giving the percent of glycol oxidized in different solvents, it is clear that of the four tertiary glycols investigated in glacial acetic acid solution, pinacone is the most difficult of all to oxidize.

The substitution of the methyl radicals in pinacol by phenyl increases the velocity of the reaction. The same rule was observed to hold for the oxidation of α-glycols in solutions of tetrachloroethane, chlorobenzene, and pyridine. Benzopinacone is to some extent different.

In the work of Griegee, there is a single scheme for the oxidation of all the glycols, independent of whether they are cis- or trans-isomers. From our point of view, the mechanism of the oxidation of cis- and trans-isomers cannot be included in the scheme for the oxidation of glycols. Our investigations (Tables 1 and 1a)** showed that, contrary to the data of Griegee:

1) No sharp difference in oxidation velocity was observed between cis- and

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*These tables appear in the second paper of this series.

**And summary table.

TABLE 1a

Cis-cyclohexanediol-1,2					Trans-cyclohexanediol-1,2				
Temperature, °C	Time, hours,	$Na_2S_2O_3$, ml	Glycol oxidized, %	Note	Temperature, °C	Time, hours,	$Na_2S_2O_3$, ml	Glycol oxidized, %	Note
50	-	0.35			50	-	0.35		
	-	0.23	34.3			-	0.35		
	1	0.23				0.5	0.28	20.0	
	2	0.23				1.0	0.26	25.8	
	6	0.23				3.0	0.20	42.9	
	7	0.27				5.0	0.15	57.2	
	8	0.48		(Formation of peroxide)		7.0	0.15	57.2	
	9	0.43							
	12	0.43			80	-	0.35		
						-	0.30	14.3	
80	-	0.35				0.25	0.19	45.7	
	-	0.15	57.2			1.00	0.09	74.3	
	0.25	0.18				1.5	0.07	80.0	
	1.00	0.38		(Formation of peroxide)		2.0	0.05	85.2	
	2.00	0.55				4.0	0.04	Practically complete oxidation	
	6.00	0.53							
	8.00	0.39							
	10	0.25			100	-	0.35		
	12	0.25				-	0.19	45.7	
						0.25	0.23		
100	-	0.35				0.50	0.33		
	-	0.14				1.0	0.34		
	0.25	0.25				2.0	0.23		
	1.0	0.54				3.0	0.12		
	2.0	0.49				3.5	0.04	Practically complete oxidation	
	4.0	0.39	Practically complete oxidation						
	8.0	0.26							
	10.0	0.19							
	13.0	0.04							

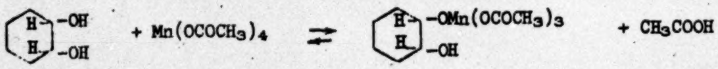
trans isomers of cyclohexanediol in acetic acid and in tetrachloroethane;

2) There is a new phenomenon, particularly in the oxidation of cis-cyclohexanediol-1,2, at 50 and 80°, in contrast to that of trans-cylcohexanediol-1,2. We observed the formation of a peroxide which was detected by the increased amount of hyposulfite used up (Table 1-a). There is a greater formation of peroxide in acetic acid solution (1-a) than in tetrachloroethane, (1-b).

3) Cis- and trans-cyclohexanediol-1,2 are oxidized more rapidly in acetic acid solution than in tetrachloroethane.

In accordance with these data, the mechanism of oxidation of cis-and trans-cyclohexanediol-1,2 may be represented by the following schemes:

a) The mechanism of oxidation of cis -cyclohexanediol-1,2:



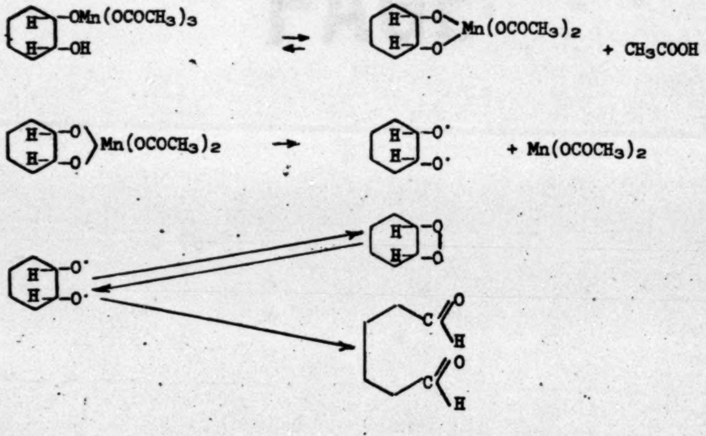
T A B L E 1-b

Cis-cyclohexanediol-1,2

Tempera-ture, °C	Time, hours	$Na_2S_2O_3$	Glycol oxidized, %
50	-	0.35	-
	-	0.28	20.0
	1.0	0.27	22.0
	2.0	0.26	25.6
80	-	0.35	
	-	0.32	10.0
	0.5	0.14	60.0
	0.75	0.11	68.9
	1.25	0.04	Practically complete oxidation
100	-	0.35	-
	-	0.24	31.5
	0.25	0.09	74.0
	0.50	0.03	Practically complete oxidation

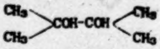
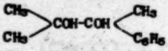
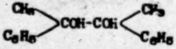
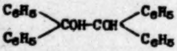
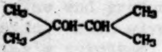
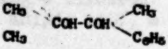
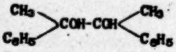
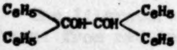
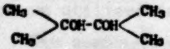
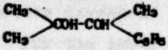
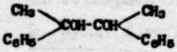
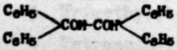
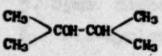
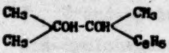
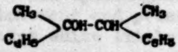
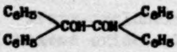
Trans-cyclohexanediol-1,2

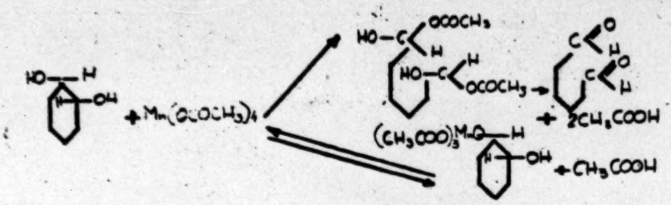
Tempera-ture, °C	Time, hours	$Na_2S_2O_3$	Glycol oxidized, %
50	-	0.35	-
	-	0.33	-
	1.0	0.32	-
	2.0	0.32	-
80	-	0.35	-
	-	0.31	11.4
	0.25	0.26	25.7
	0.50	0.25	28.6
	1.25	0.19	45.7
	2.25	0.14	60.0
	3.75	0.09	74.5
	5.75	0.03	Practically complete oxidation
100	-	0.35	-
	-	0.32	5.6
	0.25	0.11	68.9
	0.50	0.07	80.0
	0.75	0.03	Practically complete oxidation

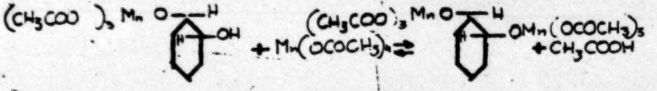


b) The mechanism of oxidation of trans-cyclohexanediol-1,2:

S U M M A R Y   T A B L E

Structural formula of glycol oxidized	Temp. °C	Acetic acid	Time heated (in hours)	Tetrachloroethane	Time heated (in hours)	Chlorobenzene	Time heated (in hours)	Pyridine	Time heated (in hours)
 $(CH_3)_2COH-COH(CH_3)_2$	20	Not oxidized	-	Not oxidized	-	Not oxidized	-	Not oxidized	-
 $(CH_3)_2COH-COH(CH_3)(C_6H_5)$	20	45.8	1.5	Same	-	Same	-	Same	-
 $(CH_3)(C_6H_5)COH-COH(CH_3)(C_6H_5)$	20	Practically complete oxidation	3.5	"	-	"	-	"	-
 $(C_6H_5)_2COH-COH(C_6H_5)_2$	20	57.2	7.0	"	-	"	-	"	-
$C_6H_5-CHOH-CHOH-C_6H_5$	20	51.5	1.5	"	-	"	-	"	-
 $(CH_3)_2COH-COH(CH_3)_2$	50	71.2	4.0	22.9	7.0	"	-	"	-
 $(CH_3)_2COH-COH(CH_3)(C_6H_5)$	50	71.5	1.5	62.0	4.5	5.6	2.25	"	-
 $(CH_3)(C_6H_5)COH-COH(CH_3)(C_6H_5)$	50	Practically complete oxidation	0.25	58.5	3.5	14.9	1.5	20.0	2.5
 $(C_6H_5)_2COH-COH(C_6H_5)_2$	50	80.0	2.5	60.0	1.5	Not oxidized	-	Not oxidized	-
$C_6H_5-CHOH-CHOH-C_6H_5$	50	Practically complete oxidation	0.5	48.6	4.0	42.9	4.0	28.6	6.0
 $(CH_3)_2COH-COH(CH_3)_2$	80	77.1	1.5	42.9	4.0	Not oxidized	-	Not oxidized	-
 $(CH_3)_2COH-COH(CH_3)(C_6H_5)$	80	Practically complete oxidation	0.5	Practically complete oxidation	2.0	42.9	4.5	17.2	6.0
 $(CH_3)(C_6H_5)COH-COH(CH_3)(C_6H_5)$	80	-	-	"	2.25	51.6	1.5	31.5	4.0
 $(C_6H_5)_2COH-COH(C_6H_5)_2$	80	Practically complete oxidation	0.5	86.1	2.0	Not oxidized	-	25.8	6.0
$C_6H_5-CHOH-CHOH-C_6H_5$	80	"	0.25	60.9	4.0	40.0	2.0	45.8	3.0
 $(CH_3)_2COH-COH(CH_3)_2$	100	-	0-	71.5	3.0	Not oxidized	-	Not oxidized	3.0
 $(CH_3)_2COH-COH(CH_3)(C_6H_5)$	100	-	0-	-	-	71.5	5.0	37.2	3.5
 $(CH_3)(C_6H_5)COH-COH(CH_3)(C_6H_5)$	100	-	0-	-	-	77.2	1.5	42.9	2.0
 $(C_6H_5)_2COH-COH(C_6H_5)_2$	100	-	0-	77.5	1.5	34.3	2.0	37.2	3.0
$C_6H_5-CHOH-CHOH-C_6H_5$	100	-	0-	65.8	1.5	65.8	2.0	39.6	2.0





The end product of the oxidation of cis- and trans-cyclohexanediol is adipic aldehyde, which gives characteristic colors with fuchsine-sulfurous acid and with Fehling's solution. After treatment with Fehling's solution, the aqueous solution gave adipic acid, m.p. 150-152°, identical with the data in the literature.

EXPERIMENTAL

The literature describes two methods for the preparation of manganese tetraacetate: from red lead and manganese acetate [5] and from manganese acetate by electrolytic oxidation in acetic acid [6].

The most suitable method appeared to be that of electrolytic oxidation, which we utilized in our work.

The compound was analyzed for its content of active oxygen. The percentage of active oxygen in our preparation was 2.89, corresponding to 53% of theory.

For the investigation, we used the following glycols:

1. Tetraphenylethylene glycol with m.p. 173-174°.
2. Symm. dimethyldiphenylethylene glycol, with m.p. 116-118°.
3. Trimethylphenylethylene glycol with m.p. 84-86°.
4. Tetramethylethylene glycol with m.p. 34-35°.
5. Symm. diphenylethylene glycol with m.p. 134-135°.
6. Cis-cyclohexanediol with m.p. 95.5-97°.
7. Trans-cyclohexanediol with m.p. 102-104°.

Cis-cyclohexanediol was obtained by the method of V.V.Markovnikov [7] from cyclohexene and potassium permanganate. After recrystallization from ligroin, shining white little leaves were obtained with m.p. 95.5-97°.

Trans-cyclohexanediol was obtained by the method of S.S.Nametkin [8] from cyclohexene oxide. The latter compound was obtained from cyclohexene and acetyl hydrogen peroxide. The melting point of the crystals obtained from water was 102-104°.

All the experiments on oxidation were carried out under the same conditions with only the temperature and solvent being changed.

The reaction was carried out in a three-necked flask with a mechanical stirrer in a stream of carbon dioxide gas (in order to avoid oxidation by oxygen of the air).

For purposes of oxidation 1/10000th of a mole of the compound to be studied was usually taken, along with the calculated amount of manganese tetracetate. In all experiments 30 ml of solvent was used. The reaction mixture was heated up to a definite temperature and after every 15 or 30 minutes in one series of experiments and 1 or 2 hours in the others, depending on the velocity of the oxidation, samples were taken for the determination of the percentage of active oxygen.

The isolation of the oxidation products of the glycols was carried out in the following manner: at the end of the oxidation, the reaction mixture was poured into water and neutralized with a 10% solution of caustic soda until it was weakly alkaline to litmus. The solution was extracted with ether, the ether extract dried over calcined sodium sulfate, and the ether then driven off.

In this oxidation, benzopinacone gave benzophenone, which was identified by the formation of an oxime with m.p. 134-136°, corresponding to the m.p. given in the literature.

The oxidation of pinacone gave acetone, which was determined quantitatively by Rudov's method [8] with sodium nitroprusside.

Symm. dimethyldiphenylethylene glycol was oxidized to give acetophenone, which was identified by the formation of an oxime with m.p. 58-59°, corresponding to the m.p. given in the literature.

Trimethylphenylethylene glycol was oxidized to give acetone and acetophenone. The acetone was detected with sodium nitroprusside, and the acetophenone by formation of an oxime with m.p. 58-59°.

Hydrobenzoin was oxidized with the formation of benzaldehyde, which was detected qualitatively with Nessler's reagent.

SUMMARY

1. It has been shown that the velocity of the oxidation of α-glycols with manganese tetracetate depends on the temperature, the solvent, and on the structure of the compound to be oxidized.

2. Of the four tertiary glycols investigated, pinacone was oxidized with the greatest difficulty.

3. The substitution of the methyl radicals in a glycol by phenyl radicals increases the tendency toward oxidation (with benzopinacone something of an exception).

4. In indifferent solvents, the process of oxidation takes place more slowly than in acetic acid.

5. Our investigations have shown that there is no great difference in the velocity of oxidation of the cis- and trans-isomers of cyclohexanediol, either in acetic acid or in tetrachloroethane.

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THE REACTION OF FORMALDEHYDE WITH AMIDES OF THE PYRIDINE SERIES

V. M. Berezovsky.

It is a known fact that the condensation of benzaldehyde with 2-dimethylaminopyridine takes place with the formation of phenyl-di-(2-dimethylamino-5-pyridyl)-methane [1]. The condensation of formaldehyde with 2-dimethylaminopyridine has not been successfully carried out, [2].

In our investigations of the reactions between formaldehyde and the amines of the pyridine series, we have shown that formaldehyde reacts with 2-dimethylaminopyridine to give di-(2-dimethylamino-5-pyridyl)-methane. This reaction increases the far from great number of cases in which a carbon atom is introduced into the pyridine nucleus. The condensation takes place with good yield in the presence of 92% formic acid or with the use of the amine hydrochloride, but does not take place with 25% hydrochloric acid.

There are several known methods for the preparation of 2-dimethylaminopyridine. The compound was obtained for the first time [3] by the action of sodium amide and methyl iodide on pyridine, then [4] by the direct methylation iwth methyl iodide of the sodium derivative of 2-aminopyridine, the separation of the reaction products (the mono- and di-methylaminopyridines) being carried out by way of the picrate. Later A.Chichibabin and I.Knunyants [5] obtained 2-dimethylaminopyridine in good yield by using the same reaction and separating the monoderivative by acetylation. They also [6] obtained good yields by using dimethyl sulfate as methylating agent. 2-Dimethylaminopyridine was also formed by the catalytic methylation of 2-aminopyridine by means of methanol vapors at 300-370° [7] and by the action of alkyl amines on 2-chloropyridine [8].

We obtained 2-dimethylaminopyridine by a new, simple, and convenient method, showing that the simultaneous action of formaldehyde and active hydrogen on 2-aminopyridine in dilute sulfuric acid solution resulted in the methylation of the amino group. In this reaction, along with the formation of a considerable quantity (28%) of the pure dimethylaminopyridine (without contamination by the secondary amine), there takes place also the formation of di-(2-dimethylamino-5-pyridyl)-methane, which is the chief product of reaction in the already known condensation [2] of formaldehyde with 2-aminopyridine in concentrated formic acid.

At the same time, we investigated the reaction of di-(2-dimethylamino-5-pyridyl)-methane with sulfur [2], the corresponding thioketone being formed. The hydrolysis of the latter compound gives di-(2-dimethylamino-5-pyridyl)-ketone, which is the starting compound in the synthesis of dyes of the di- and tripyridylmethane series [1,9]. The formation of the thioketone took place with yields up to 23% when the reaction was carried out on a small scale. An increase in the scale of the experiment led to a sharp drop in yield [10]. We have improved this reaction, and have attained yields of thioketone up to 31%, independent of the scale of the experiment.

EXPERIMENTAL

The reaction of formaldehyde with 2-dimethylaminopyridine

A mixture of 3 g of 2-dimethylaminopyridine, 4 g of 92% formic acid, and 1.4 g of 40% formalin was boiled with a reflux condenser for 7 hours. The reaction mixture was then diluted with water and made alkaline with a solution of caustic soda. The small amount of unreacted dimethylaminopyridine was then driven off by distillation with steam. The rest of the oil, after standing, was separated from the aqueous layer and washed with water. Upon cooling, the di-(2-dimethylamino--5-pyridyl)-methane crystallized. Yield 2.1 g (65%), with m.p. 76-82°.

Recrystallization from ether gave colorless little leaves with m.p. 84-85°. The compound gave a red color with hot concentrated sulfuric acid. A mixed test of the substance with known di(2-dimethylamino-5-pyridyl)-methane gave no depression of the melting point.

3.630 mg substance: 0.703 ml N_2 (23°, 750 mm).
Determination of molecular weight (Rast):
0.0049 g substance; 0.1107 g camphor: Δt 8.4°.
Found %: N 22.04; M 262.
$C_{15}H_{20}N_4$. Computed %: N 21.86; M 256.

2-Dimethylaminopyridine

A solution of 28.2 g of 2-aminopyridine in 325 g of 9% sulfuric acid was placed in a three-necked flask with a mechanical stirrer and a reflux condenser, and 65 g of 33.5% formalin was then added. Then, while stirring was continued, over the period of 1 hour there was added in small portions 120 g of zinc dust, while the temperature of the water bath was at the same time raised from 40° to 80°. The stirring was continued while the bath temperature was maintained at 80-85° for an additional 4 hours. The mixture was then cooled and filtered, and the precipitate washed well with hot water. The united filtrate and wash water were made alkaline with caustic soda and the 2-dimethylaminopyridine was driven off from them with steam. The amine was separated from the water, an equal volume of a concentrated solution of caustic soda was added to it, and the layers separated. The aqueous distillate, again distilled with steam, gave an additional small quantity of product. The yield of crude 2-dimethylaminopyridine was 11.5 g. It was sufficiently pure to be used in many reactions.

To prepare it completely pure, the crude 2-dimethylaminopyridine was dissolved in benzene, the solvent driven off, and the residue distilled in vacuum. It all distilled over at 88° at 15 mm. The yield was 10.3 g (28%).

5.090 mg substance: 1.047 ml N_2 (23°, 745 mm).
3.075 mg substance: 0.629 ml N_2 (24°, 746 mm).
Found %: N 23.25, 23.08.
$C_7H_{10}N_2$. Computed %: N 22.95.

The residue remaining from the steam distillation of the 2-dimethylaminopyridine was extracted with ether. After the solvent was driven off, there remained a base which was soluble in a small quantity of alcohol. When the alcohol was slowly evaporated, crystals gradually formed. These were filtered off and recrystallized from ligroin (80-90°). The di-(2-dimethylamino-5-pyridyl)-methane was obtained in the form of colorless little leaves, with m.p. 84-85°. In hot concentrated sulfuric acid it gave a red color. A mixed test with known di-(2-dimethylamino-5-pyridyl)-methane gave no melting point depression.

Di-(2-dimethylamino-5-pyridyl)-thioketone

Into a long-necked, round-bottomed flask there was introduced 50 g of di-(2-dimethylamino-5-pyridyl)-methane with m.p. 78-82°, and 13 g of sulfur. The flask was heated on the oil bath in a vacuum which was maintained between 10 and 15 mm all through the heating. At the beginning of the reaction, after the entire mixture had turned liquid, the flask was shaken several times. The reaction took place at a temperature of 176-180° (in the oil bath) over a period of 8 hours. An intense evolution of hydrogen sulfide took place, the liquid "boiling" energetically. At the end of the reaction, the evolution of hydrogen sulfide had almost ceased.

The reaction mixture was cooled to 100° and 35 ml of dry ethyl acetate added. After stirring, the liquid was poured into a beaker. Crystallization began after 20 to 30 minutes. After a day, the crystals were filtered off and washed in several stages with 15 ml of ethyl acetate. 21 g of violet crystals were obtained. Upon standing, the mother liquor gave an additional amount of the product. The thioketone was extracted with hot ethyl acetate (50 ml) in an apparatus of the Soxhlet type, and upon cooling, 19.35 g of product was obtained in the form of reddish violet crystals, which contained about 15% sulfur. Thus the yield amounted to 17.1 g of pure di-(2-dimethylamino-5-pyridyl)-thioketone (31%). The sulfur impurity had no influence on the preparation of the ketone from this product. Completely pure di-((2-dimethylamino-5)pyridyl)-thioketone was obtained after three recrystallizations from absolute ethyl alcohol. It had m.p. 167-167.5°. Recently published figures give the m.p. for the thioketone as 166-168° [11].

15 g of the thioketone (containing about 15% of sulfur) gave 11.5 g of the crude di-(2-dimethylamino-5-pyridyl)-ketone (yield 98-99%), or 9.5 g (83% after recrystallization from alcohol (1:6). It then had m.p. 169-170°.

0.1096 g substance: 20.6 ml N_2 (22.5°, 739 mm).
Found %: N 20.82.
$C_{15}H_{18}ON_4$. Computed %: N 20.74.

The picrate of di-(2-dimethylamino-5-pyridyl)-ketone was obtained from alcohol and recrystallized from acetone in the form of yellow needles with m.p. 184-185°.

3.645 mg substance: 0.602 ml N_2 (19°, 760 mm).
4.395 mg substance: 0.726 ml N_2 (21°, 756 mm).
Found %: N 19.31, 19.10.
$C_{15}H_{18}ON_4 \cdot 2C_6H_3O_7N_3$. Computed %: N 19.23.

SUMMARY

[1] It has been shown that di-(2-dimethylamino-5-pyridyl)-methane is obtained from 2-dimethylaminopyridine and formaldehyde.

[2] The condensation of 2-aminopyridine with formaldehyde in dilute sulfuric acid solution, under the reducing action of zinc dust, gives a considerable quantity of 2-dimethylaminopyridine. The reaction may serve as a convenient and simple method of preparation of this compound.

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AMINOALKYL ESTERS OF THIAZOLE CARBOXYLIC ACIDS

I. BENZOTHIAZOLE 2 CARBOXYLIC AND BENZOTHIAZOLE 6 CARBOXYLIC ACIDS

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The local anesthetic action of dialkylaminoalkyl esters of many organic acids (aminobenzoic, phenylacetic, α-phenylpropionic, α- and β-naphthoic, α-furancarboxylic, α-thiophencarboxylic, α-pyrrolcarboxylic, and others) gives us reason to suppose that similar esters of the series of thiazole derivatives will also have similar properties.

Such esters have been obtained for 4-methylthiazole-5-carboxylic, 2,4-dimethylthiazole-5-carboxylic, thiazolyl-4-acetic, and 2-methylthiazolyl-4-acetic acids [1]. It has been shown that these esters have spasmalytic and analgesic properties.

An investigation of thiazole carboxylic acids and their derivatives is of interest on its own account, as these compounds of the thiazole series have been comparatively little studied.

Thiazole carboxylic acids may be classified into two groups: thiazole carboxylic acids with the carboxyl in position 2 of the thiazole nucleus, and thiazole carboxylic acids with the carboxyl in any other (not in the 2) position. The first group of acids is distinguished from the other by its lesser stability. It is easily decarboxylated, splitting off carbon dioxide, and forming the corresponding thiazole.

We intended to obtain the two isomeric acids, benzothiazole-2-carboxylic acid, which is known, and benzothiazole-6-carboxylic acid, which is not described in the literature, and to synthesize the latter's aminoalkyl esters by means of the acid chloride.

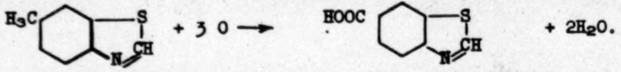
The literature gives three methods of preparation which may be used to obtain benzothiazole-2-carboxylic acid: 1) from oxalic ester, by way of thioxanilic acid [2]; 2) from o-aminothiophenol by way of 2,3-diketodihydrobenzo-1,4-thiazine [3], and 3) from 2-mercaptobenzothiazole by way of cyano-2-benzothiazole [4].

We obtained benzothiazole-2-carboxylic acid by the first and second methods. The second method was superior both with regard to speed and the convenience of carrying out the operations.

The acid chloride of benzothiazole-2-carboxylic acid was obtained in a yield 91% of theory by allowing phosphorus pentachloride to act on the acid. Ethyl alcohol and the acid chloride gave the ethyl ester, with the melting point 70-71° given in the literature [2]. With methanol, β-diethylaminoethanol, γ-diethylaminopropanol, and β-piperidinoethanol, the corresponding esters were obtained. These are not described in the literature.

Benzothiazole-6-carboxylic acid, as already indicated, has been unknown up to the present time. Its homolog, 2-methylbenzothiazole-6-carboxylic acid, has been obtained by A.Kiprianov and I.K.Ushenko [5] from 6-amino-2-methylbenothiazole by conversion into the nitrile and saponification of the latter to give the acid.

We obtained benzothiazole-6-carboxylic acid by the oxidation of 6-methylbenzothiazole with potassium permanganate in a yield about 70% of theory, according to the equation:



The 6-methylbenzothiazole needed for this reaction is known, and was obtained by the following method: p-toluidine, upon treatment with rhodanate by Kaufmann's method [6] gave 6-methyl-2-aminobenzothiazole easily and smoothly, in a quantitative yield. By cleaving the latter with a 50% aqueous solution of caustic potash at 135-150°, we obtained 6-methyl-2-aminothiophenol, which was condensed without purification with 80% formic acid. The yield of pure, distilled 6-methylbenzothiazole was 70% of theory, basing the calculation on the unpurified 6-methyl-2-aminobenzothiazole used.

The oxidation of 6-methylbenzothiazole by boiling with the calculated quantity of potassium permanganate to give benzothiazole-6-carboxylic acid did not offer any difficulties.

The acid chloride of benzothiazole-6-carboxylic acid was obtained easily (by heating the acid with thionyl chloride) in the form of the hydrochloride, with m.p. 162-164°. Treatment with an aqueous solution of sodium bicarbonate gave the free acid chloride, with m.p. 125°. Its reaction with methyl and ethyl alcohols gave the corresponding esters, and with aqueous ammonia it gave the acid amide. With β-diethylaminoethanol, γ-diethylaminopropanol, and β-piperidinoethanol it gave the diethylaminoethyl, diethylaminopropyl, and β-piperidinoethyl esters of benzothiazole-6-carboxylic acid which were of interest to us.

We had at our disposal only the β-diethylaminoethanol; the γ-diethylaminopropanol was obtained from allyl alcohol and diethylamine [7,8] and the β-piperidinoethanol from piperidine and ethylene chlorohydrin [9].

The melting point of the derivatives obtained from benzothiazole-2-carboxylic and benzothiazole-6-carboxylic acids are listed in Table 1.

The melting points and solubilities of the hydrochlorides of the esters of these isomeric acids and of the acid amides are not very different, but the melting points of the acids themselves and of their acid chlorides are different.

The aminoalkyl esters of benzothiazole-2-carboxylic and benzothiazole-6-carboxylic acids which we synthesized did not have anaesthetic properties.

EXPERIMENTAL

I. Derivatives of benzothiazole-2-carboxylic acid (I)

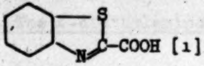
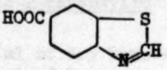
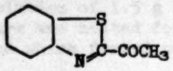
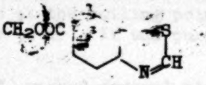
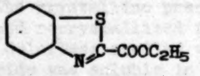
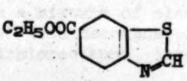
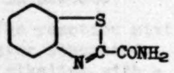
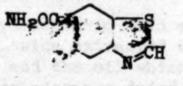
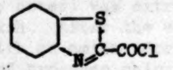
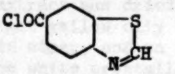
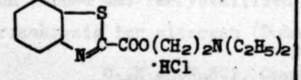
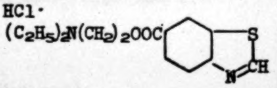
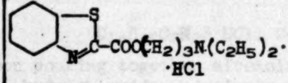
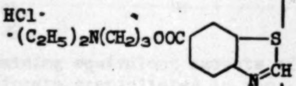
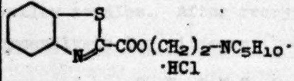
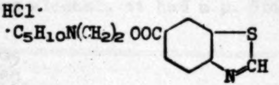
1. Benzothiazole-2-carboxylic acid

This was obtained from thioxanilic acid [2] and from o-aminothiophenol [3]. It had m.p. 108° (with decomposition).

2. The acid chloride of benzothiazole-2-carboxylic acid (V)

A mixture of 5 g of the acid with 6 g of phosphorus pentachloride (4.3% excess) was heated for 2 hours on the water bath. A faintly colored liquid was

T A B L E

No.	Compound	M.p., °	No.	Compound	M.p., °
I		108 (de-comp)	IX		245
II		90	X		103
III		70-71	XI		64
IV		228-230	XII		211
V		100-102	XIII		125
VI		184 (de-comp)	XIV		178 (de-comp.)
VII		142 (de-comp)	XV		166 (de-comp.)
VIII		192 (de-comp.)	XVI		200 (de-comp.)

formed, which solidified upon cooling. The crystalline mass was treated with ice water, and the precipitate filtered, carefully washed with water, dried in the air, and recrystallized from a small amount of benzene. The light-yellow prisms melted at 100-102° (according to the patent literature [10], the m.p. is 98-100°). The yield of crude product was 91% of theory. The acid chloride was soluble in benzene, ether, dichloroethane, and carbon tetrachloride.

Microanalysis for nitrogen (Dumas):

Found %: N 7.25.

C_8H_4ONSCl. Computed %: N 7.08.

3. The methyl (II) and ethyl (III) esters of benzothiazole-2-carboxylic acid

The methyl ester was obtained by heating the acid chloride with methyl alcohol for 30 minutes. After the alcohol had been driven off, the residue was washed with an aqueous solution of sodium bicarbonate and with water. The compound was recrystallized from very dilute aqueous alcohol. M.p. 90°.

Microanalysis for nitrogen (Dumas):
Found %: N 7.35.
$C_8H_7O_2NS$. Computed %: N 7.25.

4. The β-diethylaminoethyl ester of benzothiazole-2-carboxylic acid (VI)

To a solution of 2.5 g of the acid chloride in 15 ml of dry benzene there was added a solution of 1.5 g of β-diethylaminoethanol in 5 ml of benzene. The reaction mixture was heated for 3 hours on the water bath at the boiling point. The precipitate which formed was the hydrochloride of the ester. It was purified in two ways:

a) The crystalline precipitate was filtered off, washed several times with benzene, and recrystallized from dichloroethane or from a mixture of alcohol and acetone. Colorless needles were obtained with m.p. 184°(with decomposition). The hydrochloride was soluble in water, alcohol, and hot dichloroethane, insoluble in ether and in acetone.

b) The reaction mixture was treated with dilute hydrochloric acid and the benzene layer separated. The aqueous acid solution was twice extracted with ether, then made alkaline with a solution of sodium carbonate, and the oil which separated (the basic ester) was extracted with ether. The ether extract was dried over calcined potash. After the ether had been driven off, a light yellow oily liquid remained, with an amine odor. This liquid was dissolved in ether, and an ethereal solution of hydrogen chloride added to the solution. The white crystalline precipitate which formed was recrystallized from dichloroethane. M.p. 184°.

Microanalysis for nitrogen (Dumas):
Found %: N 8.85.
$C_{14}H_{19}O_2N_2SCl$. Computed %: N 8.90.
Determination of ionic chloride by titration (Volhard):
Found %: Cl 11.04.
$C_{14}H_{18}O_2N_2S \cdot HCl$. Computed %: Cl 11.29.

Upon pouring together alcoholic solutions containing equivalent amounts of the ester hydrochloride and picric acid, the ester picrate precipitated in the form of yellow needles. After recrystallization from alcohol, it had m.p. 162°.

Microanalysis for nitrogen (Dumas):
Found %: N 13.95.
$C_{20}H_{21}O_9N_5S$. Computed %: N 13.80.

5. The γ-diethylaminopropyl ester of benzothiazole-2-carboxylic acid (VII)

This compound was obtained in a manner similar to the preceding ester from the acid chloride and γ-diethylaminopropanol. The yield of crude product was 92% of theory. After recrystallization from a mixture of alcohol and acetone, it had m.p. 142° (with decomposition).

Microanalysis for nitrogen (Dumas):
Found %: N 8.78.
$C_{15}H_{21}O_2N_2SCl$. Computed %: N 8.52.
Determination of ionic chlorine by titration, (Volhard):
Found %: Cl 10.95.
$C_{15}H_{20}O_2N_2S \cdot HCl$. Computed %: Cl 10.80.

The picrate was obtained in the same way as before. After recrystallization from acetone it melted at 125°.

Microanalysis for nitrogen (Dumas):

Found %: N 13.34.

$C_{21}H_{23}O_9N_5S$. Computed %: N 13.43.

6. The β-piperidinoethyl ester of benzothiazole-2-carboxylic acid (VIII)

This was obtained from the acid chloride and β-piperidinoethanol. Yield of crude product was 85% of theory. It was recrystallized from a mixture of alcohol and acetone as colorless needles with m.p. 192° (with decomposition). It was readily soluble in water and alcohol.

Microanalysis for nitrogen (Dumas):

Found %: N 8.68.

$C_{15}H_{19}O_2N_2SCl$. Computed %: N 8.57.

Deterimination of ionic chlorine by titration (Volhard):

Found %: Cl 10.97.

$C_{15}H_{18}O_2N_2S \cdot HCl$. Computed %: Cl 10.86.

II. Benzothiazole-6-carboxylic acid and its derivatives

1. Benzothiazole-6-carboxylic acid (IX)

a) 6-Methyl-2-aminobenzothiazole. 20 g of powdered p-toluidine was added in portions to a carefully ground mixture of 76 g of cupric chloride and 81.6 g of potassium rhodanate. The black mass obtained was transferred to a flask, where 10 ml of acetic acid was added, and the reaction mixture was heated for 15 minutes on the water bath at 50°, with frequent shaking. It was then extracted many times with boiling water and the united aqueous extracts boiled with animal charcoal, and filtered. The filtrate was neutralized with ammonia. During this process, the 6-methyl-2-aminobenzothiazole precipitated out in the form of light-colored tiny needles, which melted at 134°. After recrystallizing from alcohol, they melted at 136°, which corresponded to the data in the literature [6]. The yield was almost quantitative.

b) 6-Methylbenzothiazole. Into an iron vessel with a capacity of 1 liter there was put 200 g of caustic potash and 200 ml of water. The solution was heated to 100°, and to it there was added 70 g of unrecrystallized 6-methyl-2-aminobenzothiazole. The solution was stirred, and heating was continued. About 135°, the reaction mixture began to froth, and a violent evolution of ammonia began. The temperature rose to 150°. Heating was continued at this temperature until there was no further evolution of ammonia. The reaction mixture was cooled to 100°, and 500 ml of water added to dissolve the entire reaction mixture. The dark-colored solution was filtered. The filtrate was neutralized with dilute hydrochloric acid, while the outside was being cooled with ice. The grayish-green precipitate of 5-methyl-2-aminothiophenol was filtered off, washed with water, carefully squeezed out, and while still moist used for the condensation reaction. For this purpose, 100 g of 80% formic acid was added to the moist precipitate, along with several small pieces of metallic zinc (in order to reduce disulfide) and the mixture was boiled for 3 hours. Upon cooling it was neutralized with a concentrated solution of caustic soda, and the 6-methylbenzothiazole which separated out was distilled with steam. The distillate was extracted with ether, and the ether extract dried with anhydrous potash. After the ether had been driven off, the residue distilled over at 251-252°. Yield 47.5 g, or 70% of theory.

c) Benzothiazole-6-carboxylic acid. In a three-necked round-bottomed flask fitted with a mechanical stirrer, a mercury seal, and a reflux condenser, there were placed 200 ml of water and 20 g of 6-methylbenzothiazole. The mixture was heated with continual stirring to the boiling point, and 40 g of potassium permanganate was added (2% excess). The heating and stirring were continued until the potassium permanganate was completely decolorized. The unreacted 6-methylbenzothiazole was distilled off with steam, and the precipitate of manganese dioxide filtered off and washed several times with hot water. The united filtrates were cooled and acidified with dilute hydrochloric acid. A crystalline precipitate of benzothiazole-6-carboxylic acid settled out. It crystallized from alcohol in the form of tablets, from acetic acid in the form of small needles. M.p. 245°, yield 11.5 g or 70% of theory, basing the calculation on the 6-methylbenzothiazole that had reacted. The unreacted 6-methylbenzothiazole was again used for the reaction. The acid was very soluble in hot glacial acetic acid, not so soluble in alcohol, very slightly soluble in water, and insoluble in dichloroethane and benzene.

Microanalysis for nitrogen (Dumas):

Found %: N 7.90.

$C_8H_5O_2NS$. Computed %: N 7.82.

Determination of equivalent weight:

Found: equivalent weight 169.

$C_7H_4NSCOOH$. Computed: equivalent weight 179.

2. The acid chloride of benzothiazole-6-carboxylic acid (XIII)

10 g of benzothiazole-6-carboxylic acid which had been recrystallized from acetic acid was boiled with 50 g of thionyl chloride on the water bath until the acid had completely dissolved. After this, boiling was continued for 30 minutes more, and the excess of thionyl chloride was driven off in the vacuum of a water jet pump. There remained a white crystalline precipitate of the hydrochloride of benzothiazole-6-carboxylic acid chloride, melting at 162-164°. The yield of crude product was 12.5 g (96% of theory). The acid chloride salt was treated with a saturated solution of sodium bicarbonate in the cold until there was no further evolution of carbon dioxide. The acid chloride precipitate was filtered off, washed with water, and dried in the air. After recrystallization from a small quantity of benzene, the compound had m.p. 125°.

Microanalysis for nitrogen, (Dumas):

Found %: N 7.22.

C_8H_4ONSCl. Computed %: N 7.08.

The acid chloride was soluble in benzene, ether, dichloroethane, and carbon tetrachloride.

3. The methyl (XI) and ethyl (XII) esters of benzothiazole-6-carboxylic acid

A mixture of 2 g of the acid chloride and 15 ml of methyl alcohol was boiled for 30 minutes. The alcohol was driven off and the crystalline precipitate treated with an aqueous solution of sodium bicarbonate, then washed with water, and recrystallized from ethyl alcohol. The yield was 1.5 g (85% of theory); m.p. 103°. The ester was soluble in hot alcohol, in hot water, in ether and in benzene. It was very slightly soluble in cold water.

Microanalysis for nitrogen (Dumas):

Found %: N 7.34.

$C_9H_7O_2NS$. Computed %: N 7.25.

The ethyl ester of benzothiazole-6-carboxylic acid was obtained in the same way as the methyl ester, and purified the same way. After recrystallization from very dilute alcohol, the compound had m.p. 64°. It was soluble in the usual organic solvents, insoluble in cold water.

Microanalysis for nitrogen (Dumas):

Found %: N 6.86.

$C_{10}H_9O_2NS$. Computed %: N 6.76.

4. The amide of benzothiazole-6-carboxylic acid (XIII)

The amide was obtained by heating the acid chloride with an aqueous solution of ammonia. After recrystallization from glacial acetic acid, it was in the form of colorless platelets. M.p. 211°. The amide was easily soluble in hot glacial acetic acid and in acetone, slightly soluble in alcohol.

Microanalysis for nitrogen (Dumas):
Found %: N 16.01.
$C_8H_6ON_2S$. Computed %: N 15.73.

5. The β-diethylaminoethyl ester of benzothiazole-6-carboxylic acid (XIV)

A solution of 2 g of diethylaminoethanol in 5 ml of benzene was added to a solution of 2.5 g of the acid chloride of benzothiazole-6-carboxylic acid in 20 ml of dry benzene. The solution, which was at first transparent, became cloudy upon heating, and gradually formed a white crystalline precipitate. The mixture was heated for 30 minutes on the boiling water bath. The residue was filtered off, washed with benzene and recrystallized from dichloroethane in the form of colorless needles with m.p. 178° (with decomposition). The yield of recrystallized product was 2.9 g (75% of theory). It was soluble in water, alcohol, and hot dichloroethane, insoluble in ether and in acetone.

Microanalysis for nitrogen (Dumas):
Found %: N 8.95.
$C_{14}H_{19}O_2N_2SCl$. Computed %: N 8.90.
Determination of ionic chlorine by titration (Volhard):
Found %: Cl 11.17.
$C_{14}H_{18}O_2N_2S \cdot HCl$. Computed %: Cl 11.29.

The picrate of the base was obtained from equiv. quan. of the hydrochloride and picric acid in alcoholic solution. After recrystallization from acetone, it had m.p. 172°.

Microanalysis for nitrogen (Dumas):
Found %: N 13.75.
$C_{20}H_{21}O_9N_5S$. Computed %: N 13.80.

6. The γ-diethylaminopropyl ester of benzothiazole-6-carboxylic acid (XV)

This was obtained in the same way as the previous ester. Yield 80% of theory, m.p. 166°.

Microanalysis for nitrogen (Dumas):
Found %: N 8.39.
$C_{15}H_{21}O_2N_2SCl$. Computed %: N 8.52.
Determination of ionic chlorine by titration (Volhard):
Found %: Cl 10.64.
$C_{15}H_{20}O_2N_2S \cdot HCl$. Computed %: Cl 10.80.

The picrate was obtained in the same way as in the preceding case. M.p. 144°.

Microanalysis for nitrogen (Dumas):
Found %: N 13.48.
$C_{21}H_{23}O_9N_5S$. Computed %: N 13.43.

7. The β-piperidinoethyl ester of benzothiazole-6-carboxylic acid (XVI)

This was obtained from the acid chloride and β-piperidinoethanol. Yield of crude product 83% of the theoretical. This recrystallized from a mixture of alcohol with acetone in the form of colorless needles with m.p. 200° (with decomposition). Very soluble in water and in alcohol.

Microanalysis for nitrogen (Dumas):

Found %: N 8.33.

$C_{15}H_{18}O_2N_2SCl$. Computed %: N 8.57.

Determination of ionic chlorine by titration (Volhard):

Found %: Cl 10.90.

$C_{15}H_{18}O_2N_2S \cdot HCl$. Computed %: Cl 10.86.

The author is profoundly grateful to Professor A.I.Kiprianov for his valuable guidance in this work.

SUMMARY

1. The β-diethylaminoethyl, γ-diethylaminopropyl, and β-piperidinoethyl esters of benzothiazole-2-carboxylic acid have been obtained.

2. Benzothiazole-6-carboxylic acid has been obtained by the oxidation of 6-methylbenzothiazole. The acid chloride of this acid has been used to synthesize the methyl, ethyl, β-diethylaminoethyl, γ-diethylaminopropyl, and β-piperidinoethyl esters, and the amide.

3. The aminoalkyl esters of these acids have no anesthetic properties.

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THE CLEAVAGE OF LIGNIN WITH METALLIC SODIUM IN LIQUID AMMONIA IV

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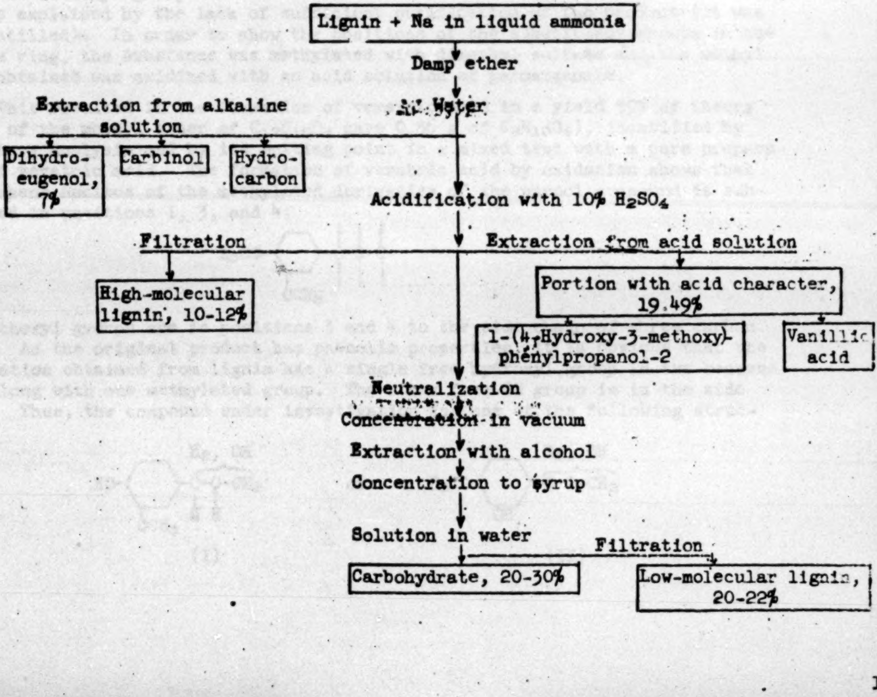
In previous communications [1,2] we have shown that the action of a solution of metallic sodium in liquid ammonia upon lignin which has been isolated from wood by the cuprammonium method, as well as by other methods (hydrochloric acid and technical hydrolysis) cleaves the lignin to form considerable amounts of monomeric phenols.

The treatment of the reaction mixture after the action of the sodium was carried out according to the given diagram:

Diagram showing separation of cleavage products


Lignin + Na in liquid ammonia
Damp ether
Water
Extraction from alkaline solution
Dihydro-eugenol, 7%
Carbinol
Hydro-carbon
Acidification with 10% H_2SO_4
Filtration
Extraction from acid solution
High-molecular lignin, 10-12%
Portion with acid character, 19.49%
1-(4-Hydroxy-3-methoxy)-phenylpropanol-2
Vanillic acid
Neutralization
Concentration in vacuum
Extraction with alcohol
Concentration to syrup
Solution in water
Filtration
Carbohydrate, 20-30%
Low-molecular lignin, 20-22%

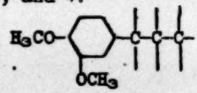
By extracting the aqueous alkali solution with ether, we obtained dihydroeugenol and monomeric neutral substances [3]. The rest of the alkaline solution was neutralized with 10% sulfuric acid until there was an acid reaction. These precipitated out of the solution the incompletely decomposed lignin (high-molecular lignin). The aqueous acid solution was extracted many times with ether. The united ether extracts were dried over sodium sulfate, and the ether distilled off. A viscous, dark-brown oil remained.

The yield of these acid low-molecular cleavage products after a single treatment of cuprammonium lignin with a solution of metallic sodium in liquid ammonia amounted to an average of 5.53% of the weight of the lignin used. Under repeated treatments of the same kin, the lignin was cleaved into the same acid products. As a result of a series of 9 treatments, a total of 19.49% of these substances was obtained, calculated on the weight of the original lignin.

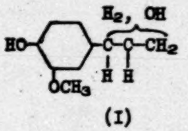
In order to separate the phenols and acids, the syrupy product was dissolved in a 5% solution of caustic soda and the phenols were precipitated from the solution by passing in a current of CO_2. The phenols which separated were extracted with ether. The ether was driven off to leave a dark-colored, transparent, thick syrup, which amounted, averaging different experiments, to 65% of the weight of the original acid products of the reaction. Thus, the amount of purified phenols amounted, after the first cleavage, to 3.6% of the weight of the original lignin, and after a series of 9 treatments to a total of 12.7% of the lignin. The product gave a green color with an alcoholic solution of ferric chloride, and showed no aldehyde reactions. When an attempt was made to distil the substance in a vacuum of 2 mm, it decomposed. Analysis of the phenolic substance for carbon and hydrogen showed that it had the composition of $C_{10}H_{14}O_3$. The substance contained a single methoxyl group and two hydroxyl groups in the molecule.

The methoxyl group content is somewhat lower than calculated theoretically; this is explained by the lack of sufficient purification of the product (it was not distilled). In order to show the positions of the substituent groups in the benzene ring, the substance was methylated with dimethyl sulfate and the methyl ether obtained was oxidized with an acid solution of permanganate.

This resulted in the formation of veratric acid in a yield 59% of theory (0.7 g of the methyl ether of $C_{12}H_{18}O_3$ gave 0.36 g of $C_9H_{10}O_4$), identified by elementary analysis and by its melting point in a mixed test with a pure preparation of veratric acid. The formation of veratric acid by oxidation shows that the benzene nucleus of the methylated derivative of the phenol compound is substituted in positions 1, 3, and 4:

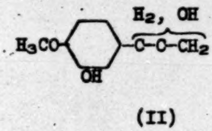


Two methoxyl groups are in positions 3 and 4 to the side chain of three carbon atoms. As the original product has phenolic properties, it is obvious that the preparation obtained from lignin has a single free hydroxyl group in the benzene ring along with one methylated group. The other free OH group is in the side chain. Thus, the compound under investigation has one of the following structures:



(I)

or



(II)

in which the position of the OH group in the side chain has not been determined. Formula (I) is more probable, as the presence of the vanillic group arrangement has more than once been demonstrated in lignin. In order further to characterize the 1-(3-methoxy-4-hydroxyphenyl)-propanol we had obtained, we prepared its derivatives.

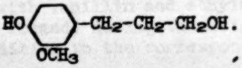
By the Schotten-Bauman reaction, the compound gave a solid benzoate with an unclearly expressed crystalline structure, melting after a 5-fold reprecipitation from alcohol in water at 90 to 95°. We could not improve this by further purification. Analysis showed: C 73.97%; H 5.95 %. Computed for the dibenzoate of 3-hydroxy-4-methoxyphenylpropyl alcohol: $C_{24}H_{22}O_5$: % C 73.83; % H 5.68.

With 3,5-dinitrobenzoyl chloride, the phenol under investigation gives a solid 3 5-dinitrobenzoate. After several recrystallizations from aqueous alcohol, a powdery product was obtained, colored light yellow. It melted at 130-145°, had % N = 9.59. Computed for the di-3,5-dinitrobenzoate of 3-hydroxy-4-methoxyphenylpropyl alcohol, $C_{24}H_{18}O_{13}N_4$: % N = 9.82.

Heating the phenol with phenyl isocyanate in toluene solution for 6 hours gave the phenylurethane, which melted after several recrystallizations from a mixture of benzene and petroleum ether at 103-108°; % N = 6.67. Computed for $C_{24}H_{24}O_5N_2$: % N = 6.66.

This investigation shows that the cleavage of lignin with metallic sodium in a solution of liquid ammonia gives 1-(4-hydroxy-3-methoxyphenyl)-propanol.

Of the three possible isomers of this compound, only one is known - dihydroconiferyl alcohol



Dihydroconiferyl alcohol was synthesized in 1928, by Nomura and Hotta [4] by the reduction, using Bouveault's method, of the ethyl ester of dihydroferulic acid. According to the data of Nomura and Hotta, dihydroconiferyl alcohol is a viscous, colorless, syrupy substance which boils at 162-163° at 5 mm. These authors obtained a dibenzoate derivative which melted at 64°.

We obtained dihydroconiferyl alcohol by two methods: 1) by the method of Nomura and Hotta, and 2) by the catalytic hydrogenation of natural coniferyl alcohol with hydrogen in the presence of Raney nickel.

In both cases, the product boiled at 162-163° at 5 mm, which corresponded to the data of Nomura and Hotta. However, in contradistinction to the compound of Nomura and Hotta, which was in liquid form, the dihydroconiferyl alcohol which we had obtained by two methods was a white solid substance with m.p. 65-70°. The dibenzoate melted sharply at 64°, and the phenylurethane at 124-126°, which corresponded with complete accuracy to the data of Nomura and Hotta. The derivatives of the synthetic dihydroconiferyl alcohol gave no melting point depression when mixed with derivatives of the hydrogenated coniferyl alcohol.

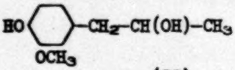
A comparison of the properties of the phenol compound isolated from lignin after decomposition with metallic sodium in liquid ammonia with the properties of the synthetic dihydroconiferyl alcohol makes it obvious that the derivatives of these two compounds have different melting points.

We might make the assumption that polymorphism is present. This might be done for several reasons, especially in connection with the polymorphism observed by Kawai and Sugiyama [5] for the bis-para-nitrobenzoate of dihydroconiferyl alcohol. This derivative, prepared from natural dihydroconiferyl alcohol, melted at 113-113.5°, while the bis-para-nitrobenzoate from synthetic dihydroconiferyl alcohol had m.p. 121-121.5°. Upon melting, the first form was transformed into the second.

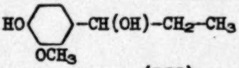
But in our case, it is impossible to explain the lack of correspondence between melting points by polymorphism, as we observed no transition from one form into the other. Thus, we must note that the 1-(4-hydroxy-3-methoxyphenyl)-propanol which we had obtained from lignin was not identical with dihydroconiferyl alcohol, but was only its isomer.

In favor of this conclusion, there is also the fact that a considerable amount of acetic acid (73% of theory) is formed by the oxidation of the phenolic product from lignin with chromic acid. Parallel experiments, carried out under the same conditions with dihydroeugenol, gave acetic acid in 74% yield, while dihydroconiferyl alcohol gave not even traces of acetic acid. These results indicate the presence on the end of the side chain of the substance under investigation of a CH_3 group, and not of a CH_2OH group [6].

The two other isomers of 1-(4-hydroxy-3-methoxyphenyl)-propanol (II and III)



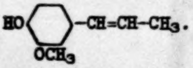
(II)



(III)

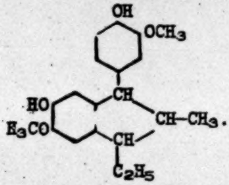
had up to the present time not been obtained.

We synthesized isomer III – 1-(4-hydroxy-3-methoxyphenyl)-propanol-1. The synthesis was carried out with vanillin and ethylmagnesium bromide. It is known that in this case there is formed, during the Grignard reaction, as a result of the dehydrogenation, in addition to the corresponding secondary alcohol, isoeugenol [7,8]:



However, Behal and Tiffeneau [7], who obtained these results, carried out the reaction in such a way that after they added the vanillin to the Grignard reagent (3 moles per mole of vanillin) they heated the reaction mixture to 105°.

We found that the action of two molecules of ethylmagnesium bromide on 1 molecule of vanillin (1 molecule for the reaction with the aldehyde group and 1 for the phenolic OH group), followed by heating on a water bath for 1 hour, gave an almost quantitative yield of the substance $C_{20}H_{24}O_4$, which melted at 181°, boiled at 220°, at 4 mm, and gave a benzoate with m.p. 161°. It appeared to be diisoeugenol, whose structure was determined by Müller and Horwath [9]:



Thus, during the Grignard reaction there took place the dehydration of the alcohol first formed, and condensation of the isoeugenol obtained, a result which Behal and Tiffeneau did not observe.

When 1.5 moles of C_2H_5MgBr was allowed to react with vanillin, without subsequent heating, we obtained a viscous, syrupy substance which decomposed upon distillation in vacuum. This substance gave a mixture of two benzoates, which were easily separated by recrystallization into individual pure products: the first benzoate was very soluble in alcohol, the second benzoate was insoluble in alcohol. After 5 recrystallizations from alcohol, the first substance melted at 112-117°, had % C = 74.15, % H = 6.01. Computed for the dibenzoate of 1-(3-methoxy-4-hydroxyphenyl)-propanol, $C_{24}H_{22}O_5$: % C 73.83; % H 5.69.

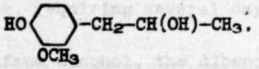
The dibenzoate was a white powdery substance with an unclearly expressed crystalline structure, and a far from sharp melting point. In solubility and appearance this benzoate was extraordinarily similar to the dibenzoate of the 1-(4-hydroxy-3-methoxyphenyl)-propanol obtained from lignin by cleavage with metallic sodium in liquid ammonia. The melting points, however, differed.

The second dibenzoate obtained from the product of the Grignard reaction melted at 189°. This substance was not investigated.

The 1-(4-hydroxy-3-methoxyphenyl)-propanol-1 which we had synthesized by the Grignard method gave a diphenylurethane which melted, after 5 recrystallizations from a mixture of benzene and petroleum ether, at 110-115°; % N = 7.01. Computed for $C_{24}H_{24}O_5N_2$: % N = 6.66.

The diphenylurethane of 1-(4-hydroxy-3-methoxyphenyl)-propanol-1, judging from external appearance (fine white grains) and solubility was also very similar to the diphenylurethane of the 1-(4-hydroxy-3-methoxyphenyl)-propanol obtained from lignin; however, the melting point of the latter was lower.

It is obvious that the phenolic compound from lignin very closely resembles in its properties the 1-(4-hydroxy-3-methoxyphenyl)-propanol-1 which we synthesized. However, despite the uncharacteristic, drawn-out melting points of the dibenzoates and the diphenylurethanes of both compounds, the melting points of the derivatives differ from each other sufficiently to force us to assume a difference in their structure. Consequently, the 1-(4-hydroxy-3-methoxyphenyl)-propanol obtained by the decomposition of lignin is the III isomer, that is, 1-(4-hydroxy-3-methoxyphenyl)-propanol-2:



EXPERIMENTAL

The preparation of the methyl ester of the phenolic compound isolated from lignin

2 g of the phenolic compound was dissolved in 22.3 ml of a 2 N solution of caustic potash. The solution was heated gradually on the water bath, and to it there was added from a dropping funnel twice the theoretically calculated amount of dimethylsulfate. Then there were added, in turn, portions of the 2 N caustic potash solution and dimethylsulfate in amounts 1/2 and 1/4 of that added previously.

At the end of the reaction, the mixture was heated for an additional hour. The methylated product was extracted from the weakly alkaline solution with ether. The ether extract was dried over sodium sulfate, and the ether driven off. The yellow oil which remained had a characteristic caraway odor. The yield amounted to 80% of the amount of phenol used. The preparation was distilled in vacuum. It boiled at 135-140° at 3-4 mm pressure.

The oxidation of the methyl ether of the phenol

0.75 g of the methyl ether of the phenol was dissolved in 5 ml of acetone. The acetone solution was poured into 50 ml of water in a three-necked flask, while energetic stirring was carried on. A fine emulsion of the substance was formed in the water. The solution was heated to 95° for 1.5 hours in order to remove acetone completely, and the mixture was then cooled to 60°. Powdered $KMnO_4$ was added in small portions until there was no further decolorization. A total of 3.6 g of $KMnO_4$ was used up in the reaction.

The manganese dioxide was removed by filtration, and the solution was acidified with 10% sulfuric acid and the acids formed extracted with ether. The ether extract was dried over anhydrous sodium sulfate, and the ether driven off. A thick syrupy oil remained. The volatile ethereal acids were removed by standing in a dessicator over soda-lime. The residue was treated with small portions of hot benzene. The cooled benzene extracts were filtered, the benzene driven off, and the crystalline mass remaining was recrystallized twice from water. The product obtained was in the form of fine white needlelike little crystals, with m.p. 178-179°. The yield of acid amounted to 59% of theory. A mixed test with veratric acid gave no melting point depression. M.p. 177-179°.

5.3 mg substance: 11.57 mg CO_2; 2.76 mg H_2O.
6.92 mg substance: 15.06 mg CO_2; 3.71 mg H_2O.
Found %: C 59.53, 59.37; H 5.79, 6.00.
(veratric acid) $C_9H_{10}O_4$. Computed %: C 59.37; H 5.54.

The preparation of the dibenzoate of the 1-(4-hydroxy-3-methoxyphenyl)-propanol isolated from lignin

The dibenzoate was obtained by the Schotten-Baumen method, slightly altered. A 20% solution of caustic soda was used. One part of the phenolic compound was dissolved in 50 parts of 20% caustic soda. To the solution there were added 6 parts of benzoyl chloride, and the reaction mixture was shaken at 25° until the odor of benzoyl chloride had disappeared. The light yellow solid mass which precipitated was treated many times with water at the boiling point. The dibenzoate was then obtained in the form of a slightly yellow powder. (The product occasionally failed to harden at once, requiring several days of standing in the water).

After 5 reprecipitations from alcohol, the dibenzoate was obtained in the form of a white powder with a somewhat drawn-out melting point, 90-95°.

3.48 mg substance: 9.45 mg CO_2; 1.90 mg H_2O.
3.30 mg substance: 8.94 mg CO_2; 1.72 mg H_2O.
Found %: C 74.06, 73.90; H 6.11, 5.80.
$C_{24}H_{22}O_5$. Computed %: C 73.83; H 5.68.

The preparation of the bis-3,5-dinitrobenzoate of the 1-(4-hydroxy-3-methoxyphenyl)-propanol from lignin

0.4 g of the phenol and 1 g of 3,5-dinitrobenzoyl chloride were dissolved in 10 ml of pure pyridine. The reaction mixture was boiled with a reflux condenser for 1 hour. After cooling, 40 ml of 5% sulfuric acid was added to the flask. The reaction product gradually precipitated in the form of a viscous paste. It was extracted with ether and the ethereal solution washed with water. The ether was driven off to leave a solid yellow mass. The product was recrystallized several times from aqueous alcohol. It was then obtained in the form of a light yellow powdery substance with melting range from 130-145°.

5.456 mg substance: 0.459 ml N_2 (19°, 744.0 mm).
4.275 mg substance: 0.362 ml N_2 (21.3°, 740.1 mm).
Found %: N 9.62, 9.57.
$C_{24}H_{18}O_{13}N_4$. Computed %: N 9.82.

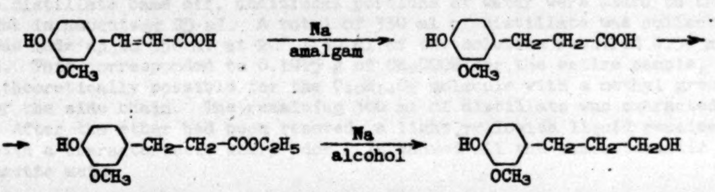
The preparation of the diphenylurethane of the 1-(4-hydroxy-3-methoxyphenyl)-propanol from lignin

The substance under investigation was boiled for 6 hours with twice the euqivalent of phenyl isocyanate in toluene. The product was treated with gasoline three times to remove the unreacted phenyl isocyanate. The diphenylurethane obtained was recrystallized 5 times from a mixture of benzene and petroleum ether. It was a white powdery substance with m.p. 103-108°.

3.590 mg substance: 0.218 ml N_2 (24°, 726 mm).
Found %: N 6.67.
$C_{24}H_{24}O_5N_4$. Computed %: N 6.66.

The synthesis of dihydroconiferyl alcohol

The work was carried out by the method described by Nomura and Hotta:



The properties of the intermediate products and the yields corresponded to the description. The dihydroconiferyl alcohol obtained was distilled at 162-163° at 5 mm. It hardened after the distillation to give a solid mass which melted at 65-70°.

8.637 mg substance: 21.052 mg CO_2; 6.080 mg H_2O.
5.872 mg substance: 14.314 mg CO_2; 4.137 mg H_2O.
Found %: C 66.47, 66.49; H 7.82, 7.84.
$C_{10}H_{14}O_3$. Computed %: C 65.91; H 7.43.

Benzoate: m.p. 63-64°. White, well formed crystals.

4.709 mg substance: 12.799 mg CO_2; 2.425 mg H_2O.
6.381 mg substance: 17.329 mg CO_2; 3.189 mg H_2O.
Found %: C 74.13, 74.06; H 5.72, 5.55.
$C_{24}H_{22}O_5$. Computed %: C 73.83; H 5.68.

Diphenylurethane: m.p. 124-126°.

3.47 mg substance: 0.222 ml N_2 (24°, 741 mm).
Found %: N 7.12.
$C_{24}H_{24}O_5N_2$. Computed %: N 6.66.

The hydrogenation of coniferyl alcohol in the presence of Raney nickel

3 g of coniferyl alcohol was dissolved in 10 ml of C_2H_5OH. The solution was shaken with 0.5 g of Raney nickel in an atmosphere of electrolytic hydrogen. The reaction took place over a period of 4.5 hours. 869 ml of hydrogen were absorbed. The solution was filtered from the catalyst and extracted with ether. After the solvent had been driven off, the material was in the form of a very viscous, light yellow colored oil. It boiled at 163-165° at 5 mm and hardened to give a white

mass, with m.p. 66-70°. It gave no depression of the melting point with synthetic dihydroconiferyl alcohol. It gave a benzoate with m.p. 64-65°.

A mixed test of the latter with the dibenzoate of dihydroconiferyl alcohol gave m.p. 64-65°. The diphenylurethane melted at 124°.

3.770 mg substance: 0.214 ml N_2 (24°, 739 mm).
Found %: N 6.36.
$C_{24}H_{24}O_5N_2$. Computed %: N 6.66.

The oxidation of the 1-(4-hydroxy-3-methoxyphenyl)-propanol from lignin with chromic acid

To 0.8 g of the phenolic substance from lignin there was added by means of a dropping funnel a solution of 30 g of CrO_3 in 75 ml of water. The work was carried out in a current of nitrogen. The bath temperature was gradually raised to 160°, and 25 ml of water was then added to the reaction mixture. The reflux condenser was replaced by a direct condenser, and the distillate collected in a receiving vessel, which was protected from the carbon dioxide of the air by means of a large tube filled with soda lime.

As the distillate came off, additional portions of water were added to the reaction flask in amounts of 25 ml. A total of 330 ml of distillate was collected. The volume was made up to 350 ml at 20°. 50 ml of the solution required 4.56 ml of 0.1 N KOH. This corresponded to 0.1915 g of CH_3COOH for the entire sample, or 73% of that theoretically possible for the $C_{10}H_{14}O_3$ molecule with a methyl group at the end of the side chain. The remaining 300 ml of distillate was extracted with ether. After the ether had been removed, a light yellowish liquid remained (0.162 g), with a characteristic sharp odor. It showed all the characteristic reactions of acetic acid.

The oxidation of dihydroconiferyl alcohol

0.260 g of the substance was used for the oxidation. The work was carried out under the same conditions as before. With this compound no acid reaction was observed in the distillate. After the ether was driven off, no acetic acid was detected in the residue.

The synthesis of 1-(4-hydroxy-3-methoxyphenyl)-propanol-1

1) 4.8 g of mangesium shavings were placed in a three-necked flask fitted with a stirrer, and 21.5 g of C_2H_5Br in 50 ml of absolute ether was added. At the end of the reaction, a solution of vanillin (15 g) in absolute ether was added to the Grignard reagent. A white precipitate was immediately formed, and by the end of the reaction, the entire mass had hardened. At the end of the addition of the vanillin, the reaction mixture was heated for 1 hour on the water bath. The mixture was decomposed with ice and hydrochloric acid (15 ml). The reaction product was extracted with ether, and the ether extract shaken numerous times with an aqueous solution of sodium bisulfite. The ether extract was then dried and the solvent driven off. The mass that remained hardened. After 3 recrystallizations from alcohol, the substance melted at 181°. It was in the form of beautiful, fine white needles. B.p.220° at 4 mm.

4.190 mg substance: 11.173 mg CO_2; 2.825 mg H_2O.
Found %: C 72.73; H 7.49.
$C_{20}H_{24}O_4$. Computed %: C 73.17; H 7.37.
(diisoeugenol)

After recrystallization from benzene, the benzoate was in the form of fine crystals with m.p. 161°.

8.56 mg substance: 23.87 mg CO_2; 4.79 mg H_2O.
8.15 mg substance: 22.70 mg CO_2; 4.39 mg H_2O.
Found %: C 76.10, 76.01; H 6.22, 6.02.
$C_{34}H_{32}O_6$. Computed %: C 76.10; H 6.01.
(diisoeugenol dibenzoate)

2) 15 g of vanillin, 18.7 g of C_2H_5Br and 4.2 g of magnesium were used. After the vanillin solution had all been added to the ether, the reaction mixture was immediately decomposed with ice and hydrochloric acid. Further treatment of the reaction mixture was carried out as in the first experiment. After the ether had been driven off from the ether extract, the remaining solvent was removed in a vacuum dessicator in the cold. The reaction product was in the form of a light yellow, very viscous syrup, which did not crystallize even upon prolonged standing and rubbing with a glass stirring rod. Upon standing in the air, it gradually hardened.

The benzoate. The benzoate was prepared by the Schotten-Bauman reaction. It was easily split up into two different substances: a) soluble in alcohol, and b) insoluble in alcohol, but soluble in benzene. The product b) was in the form of a white crystalline material with m.p. 189°. It was not investigated further.

Substance a) was recrystallized five times from alcohol. It was in the form of a white powdery substance with m.p. 112-117°.

10.74 mg substance: 29.25 mg CO_2; 5.964 mg H_2O.
Found %: C 74.27; H 6.17.
11.24 mg substance: 30.56 mg CO_2; 6.07 mg H_2O.
Found %: C 74.15; H 6.01.
$C_{24}H_{22}O_5$. Computed %: C 73.83; H 5.69.

The diphenylurethane. 0.3 g of the substance was boiled with 0.5 g of phenyl isocyanate in 10 ml of toluene for 6 hours. The solvent was driven off, and the residue (an oily product) was subjected to three treatments with gasoline at the boiling point. The solid substance obtained was recrystallized 5 times from a mixture of benzene and gasoline. The white material had a grainy structure. M.p. 110-115°.

3.565 mg substance: 0.219 ml N_2 (24°, 755 mm).
Found %: N 7.01.
$C_{24}H_{24}O_5N_2$. Computed %: N 6.66.

SUMMARY

1. The decomposition of cuprammonium lignin with metallic sodium in liquid ammonia gave, in addition to other monomeric substances, about 13% of a phenolic substance which was extracted with ether from the acid aqueous solution.

2. The following derivatives of this substance were obtained and characterized: the dibenzoate, the bis-phenylurethane, and the bis-3,5-dinitrobenzoate.

3. It has been shown that the substance isolated is 1-(4-hydroxy-3-methoxyphenyl)-propanol-2.

4. The synthesis of dihydroconiferyl alcohol from ferulic acid, performed in 1929 by Nomura and Hotta, has been repeated. It has been found that dihydroconiferyl alcohol is a solid substance with m.p. 65-70°, and not a syrupy liquid, as described by Nomura and Hotta.

5. Dihydroconiferyl alcohol has been obtained by the catalytic hydrolysis of coniferyl alcohol.

6. 1-(4-Hydroxy-3-methoxyphenyl)-propanol-1 has been synthesized for the

first time from vanillin and ethylmagnesium bromide. It has been found that when the vanillin is made to react with 1.5 moles of C_2H_5MgBr without subsequent heating, the reaction proceeds normally, without the dehydration of the secondary carbinol formed.

7. The reaction of vanillin with two moles of C_2H_5MgBr , followed by heating, gives diisoeugenol.

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December 7, 1948.

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* See CB translation p. 1095 ff. and p. 1569 ff.

ON SEVERAL DERIVATIVES OF PHENANTHRENE

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This work was begun before the war. Its objective was to investigate various unsaturated compounds of the phenanthrene series. But during the war, our preparations were lost, and being unable to turn back to the work that had been interrupted, we are publishing those results which appear new, and in particular the results on the synthesis and properties of various alcohols containing phenanthrene radicals, not yet described in the literature.

These alcohols were obtained by the Grignard reaction, from phenanthrylmagnesium bromide and the corresponding aldehydes or ketones. We synthesized:

Ethyl-9-phenanthrylcarbinol	m.p. 102°
Dimethyl-9-phenanthrylcarbinol	m.p. 77-78°
Propyl-9-phenanthrylcarbinol	m.p. 107.5-108°
Methylethyl-9-phenanthrylcarbinol	m.p. 106°
Isopropyl-9-phenanthrylcarbinol	m.p. 99-100°.

In addition, during the synthesis of methyl-9-phenanthrylcarbinol we obtained crystals with m.p. 190°, apparently α-phenanthrylethylphenanthryl ether.

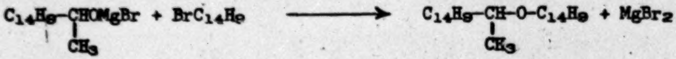
EXPERIMENTAL

Phenanthrylmagnesium bromide. Bergmann [1] and Bachmann [2] prepared phenanthrylmagnesium bromide in benzene solution, using iodine to initiate the reaction. We found it more suitable to use a small amount of ethylmagnesium bromide for this purpose. In a small test tube, we placed 2-3 ml of dry ether, 2 ml of ethyl bromide, and several shavings of magnesium. As soon as the reaction began, the contents of the test tube were added to a flask containing 58 g of bromo-9-phenanthrene, 5.4 g of magnesium, and 150 ml of ether. The reaction began immediately and proceeded so energetically that it had to be slowed down by the addition of 150 ml of dry benzene. The magnesium dissolved in 50 to 60 minutes, instead of the 4 to 5 hours needed with iodine.

Phenanthrylmagnesium bromide and acetaldehyde. To a solution of phenanthrylmagnesium bromide there was added, with cooling, 16 ml of acetaldehyde in 35 ml of ether. After 7 hours, the mixture was decomposed with dilute sulfuric acid. After part of the solvent had been driven off, 35 g of methyl-9-phenanthrylcarbinol was obtained with m.p. 133-134°, [2]. The yield was 70% of the theoretical. The mother liquor gave 1.5 g of crystals with m.p. 190°. This gave no reaction for the hydroxyl group by Tserevitinov's method.

0.1598 g substance: 0.5302 g CO_2; 0.9960 g H_2O.
0.1304 g substance: 19.66 g benzene: Δt 0.083°.
Found %: C 90.40; H 6.9; M 407.5.
$C_{30}H_{22}O$. Computed %: C 90.40; H 5.57; M 397.2.

Apparently this was α-phenanthrylethylphenanthryl ether, formed by the following reaction:



$$C_{14}H_9\underset{CH_3}{-CH}OMgBr + BrC_{14}H_9 \longrightarrow C_{14}H_9\underset{CH_3}{-CH}-O-C_{14}H_9 + MgBr_2$$

Ethyl-9-phenanthryl carbinol. To a solution of phenanthrylmagnesium bromide prepared from 52 g of 9-bromophenanthrene and 4.8 g of magnesium, there was added with cooling 16 g of propionic aldehyde in 15 ml of ether. After 3 hours, the mixture was decomposed with dilute sulfuric acid. The ether was driven off to leave an oil, which quickly hardened to give crystals. These were pressed on a porcelain plate. Yield 25 g (52.5% of the theoretical). After crystallization from a mixture of ethyl acetate and petroleum ether, the melting point was 102°.

0.1098 g substance: 0.3480 g CO_2; 0.0688 g H_2O.
0.1536 g substance: 19.0 g benzene: Δt 0.178°.
Found %: C 86.43; H 7.01; M 231.5.
$C_{17}H_{16}O$. Computed %: C 86.37; H 6.83; M 236.1.
0.0786 g substance: gave (Tserevitinov) 8.40 ml of ethane (19°, 740 mm).
$C_{17}H_{15}(OH)$. Computed 8.13 ml ethane.

The substance dissolved with difficulty in petroleum ether and ligroin, but dissolved well in other organic solvents.

Dimethyl-9-phenanthryl carbinol. This was synthesized in the same manner as the preceding compound, with an equivalent quantity of acetone replacing the aldehyde. The alcohol obtained was recrystallized from petroleum ether in the form of snow-white needles with m.p. 77-78°.

0.1552 g substance: 0.4894 g CO_2; 0.1068 g H_2O.
0.1480 g substance: 21.27 g benzene: Δt 0.159°.
Found %: C 86.0; H 7.70; M 228.9.
$C_{17}H_{16}O$. Computed %: C 86.37; H 6.83; M 236.1.
0.1064 g substance: gave (Tserevitinov) 10.9 ml ethane (22°, 763.3 mm).
$C_{17}H_{15}(OH)$. Computed: ethane 10.9 ml.

This alcohol, being a tertiary alcohol, lost water even when distilled in vacuum, forming isopropenylphenanthrene $(C_{14}H_9)(CH_3)C{=}CH_2$, with b.p. 172-174° at 4 mm. It gave a picrate with m.p. 108°, which corresponded to the data of E. and F. Bergmann [1].

1.1944 g substance: 0.6637 g CO_2; 0.1090 g H_2O.
Found %: C 93.11; H 6.27.
$C_{17}H_{14}$. Computed %: C 93.51; H 6.48.

n-Propyl-9-phenanthrylcarbinol. This was prepared in the manner described above from 35 g of phenanthrene, 3.25 g of magnesium, and 10 g of n-butyraldehyde. 18.5 g of crystals were obtained (53% of theory). After recrystallization from petroleum ether and then from a mixture of chloroform and petroleum ether, these melted at 107-108°. They were in the form of fine, shining needles, soluble in the usual organic solvents, soluble with more difficulty in petroleum ether and ligroin.

0.1358 g substance: 0.4272 g CO_2; 0.0919 g H_2O.
0.1608 g substance: 20.02 g benzene: Δt 0.170°.
Found %: C 85.78; H 7.56; M 251.8.
$C_{18}H_{18}O$. Computed %: C 86.35; H 7.25; M 250.1.

Methylethyl-9-phenanthrylcarbinol. To a solution of phenanthrylmagnesium prepared from 58 g of bromophenanthrene and 5.4 g of magnesium, there was added quickly, in 5 to 8 minutes, 22 g of methylethylketone in 30 ml of ether. A finely crystalline precipitate of the alcoholate was formed. After a half hour, the mixture was treated with dilute sulfuric acid. This gave an oil, which quickly crystallized. The yield of crystals pressed out on a porcelain plate was 29 g (51% of the theoretical). The crystals were dissolved in acetone and precipitated with petroleum ether, then recrystallized from petroleum ether. M.p. 106°. The compound was very soluble in chloroform, acetone, and ethyl acetate, soluble with difficulty in ethyl and cold methyl alcohol.

0.1636 g substance: 0.5169 g CO_2; 0.1040 g H_2O.
0.1640 g substance: 19.81 g benzene: Δt 0.166°.
Found %: C 86.15; H 7.13; M 254.3.
$C_{18}H_{18}O$. Computed.%: C 86.35; H 7.25; M 250.1

Isopropyl-9-phenanthrylcarbinol. The synthesis of this alcohol was carried out in the same manner as that of methylethylphenanthrylcarbinol, using isobutyraldehyde in place of the methylethylketone. The reaction mixture was allowed to stand overnight. The bottom of the flask appeared covered with white crystals of the alcoholate. The benzene-ether layer was poured out. Its treatment gave none of the product sought, but decomposition of the crystalline precipitate gave a product which appeared to be the expected carbinol. After crystallization from ligroin it melted at 99-100° (a mixed test with phenanthrene gave a melting point of 65°). The compound was very soluble in ether and in benzene, slightly soluble in ligroin.

0.1538 g substance: 0.4903 g CO_2; 0.1019 g H_2O.
0.1880 g substance: 19.78 g benzene: Δt 0.192°.
Found %: C 86.95; H 7.41; M 252.4.
$C_{18}H_{18}O$. Computed %: C 86.35; H 7.25; M 250.1.
0.1876 g substance gave (Tserevitinov) 17.60 ml ethane (21°, 762 mm).
$C_{18}H_{17}(OH)$. Computed: 18.05 ml ethane.

SUMMARY

The synthesis and properties of five alcohols containing phenanthryl radicals have been described, and it has been noted that the synthesis of methylphenanthrylcarbinol gives as a byproduct α-phenanthrylethylphenanthryl ether.

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ON THE OXIDATION OF β METHYLCYCLOHEXANONE

THE SYNTHESIS OF 1 METHYL 3 PROPYLCYCLOPENTANE

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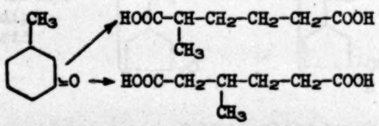
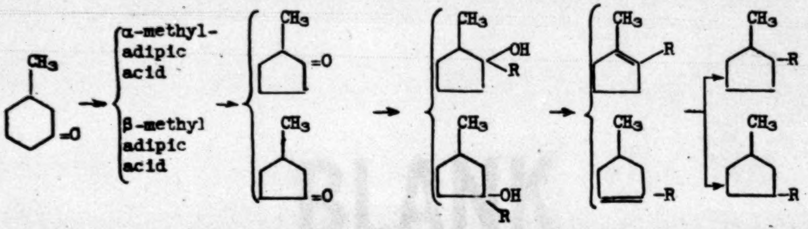
It is easy to show that the oxidation of β-methylcyclohexanone can give α- and β-methyladipic acids:



Various investigations, whose results do not completely agree with each other, have been devoted to this reaction. In 1886 Wallach [1] found among the products of the oxidation of β-methylcyclohexanone with an alkaline permanganate solution, in addition to β-methyladipic acid, an acid with m.p. 69°, which he considered to be the α-acid. In 1900 Markovnikov [2] oxidized β-methylcyclohexanone with nitric acid, to obtain an organic acid with m.p. 52-53°. He believed that in this case oxidation took place exclusively in a way to form the α-methyladipic acid. In 1901 Bouveault and Tetry [3] oxidized β-methylcyclohexanone by the same method, and obtained from the products of oxidation the diamides of acids, which they thought they had separated by crystallization into the diamide of the α-acid and the diamide of the β-acid. However, they did not succeed in confirming the presence of the α-isomer derivative. In 1902 Speransky [4] attempted to separate the oxidation products of β-methylcyclohexanone by converting them into a mixture of α- and β-methylcyclopentanones and condensing the latter with benzaldehyde. α-Methyladipic acid was supposed to give α-methylcyclopentanone, and the latter a monobenzylidene derivative; the β-acid was supposed to give the corresponding β-methylcyclopentanone and a dibenzylidene derivative. Speransky was able to obtain only the latter compound. Finally, in 1903 Markovnikov [5] again turned to the oxidation of β-methylcyclohexanone with nitric acid and showed that Bouveault and Tetry were mistaken: crystallization of the dianilides obtained from the products of oxidation enabled him to show the presence of both the α- and the β-methyl adipic acids, which were, according to Markovnikov, in approximately equal amounts. In later years, no attention was paid to the oxidation of β-methylcyclohexanone for the purpose of obtaining methyladipic acids.

Among other things, this reaction may be utilized for the synthesis of disubstituted homologs of cyclopentane in which one of the substituents is methyl, if the methyladipic acids formed by oxidation are not separated, but converted into a mixture of α- and β-methylcyclopentanes, and the latter by the Grignard reaction, into a mixture of tertiary alcohols. Dehydration of the alcohols gives a mixture of the corresponding 1,2- and 1,3- disubstituted cyclopentenes. Judging by the results of Chavanne [6], the dehydration of 1,2-dimethylcyclopentanol-1 gives 1,2-dimethylcyclopentene-1 exclusively. The dehydration of 1,3-dimethylcyclopentanol-1, as is shown in the experimental section of this work, also gives only a single dimethylcyclopentene, with a single boiling point, and apparently with the structure of 2,4-dimethylcyclopentene-1. The first of these hydrocarbons has a somewhat higher boiling point than the second, which makes it possible to separate them completely by distillation with a sufficiently effective column. Allowing for the fact that there are similar differences in boiling point not only for 1,2- and 1,3-dimethylcyclopentenes, but for other disubstituted cyclopentenes as well which contain a single methyl group as substituent, we can construct the following scheme for the synthesis of the 1,2- and 1,3- disubstituted homologs of cyclopentane, in which one of the substituents is methyl and the other any other alkyl:



This scheme has been successfully applied by us to the synthesis of 1,2- and 1,3-dimethylcyclopentanes and 1-methyl-3-propylcyclopentane. 1-Methyl-2-propylcyclopentene, obtained in this manner, was converted by us into 1-methyl-2-propylcyclopentane because its amount appeared very small.

In contradistinction to Markovnikov, who carried out the oxidation of β-methylcyclohexanone with a large excess of concentrated nitric acid, we carried it out with a small excess of nitric acid somewhat diluted with water, in the presence of ammonium metavanadate. The amount of β-methyladipic acid formed in our experiments was always greater than the amount of α-acid, as can be seen from the relative yields of the 1,2- and 1,3-disubstituted cyclopentenes.

The hydrogenation of the fractionally distilled 1-methyl-3-propylcyclopentene was carried out both in the vapor phase in the presence of platinized charcoal and in alcoholic medium with the same catalyst in the presence of H_2PtCl_6 and a considerable amount of hydrochloric acid. In both cases, the saturated hydrocarbon was obtained, 1-methyl-3-propylcyclopentane, with completely identical constants. The spectra for the combined scattering of light, determined by M.I.Batuev, also showed the identity of the product in both cases. Thus, we were not able to obtain any indication of the existence of steric isomers of 1-methyl-3-propylcyclopentane.

1-Methyl-3-propylcyclopentane was first described by N.D.Zelinsky and V.V. Chelintsev in 1903, in a short note [3]. They found:

B.p. 146-148° (760 mm); $d_4^{17.5}$ 0.7725; $[\alpha]_D + 3.10°$; method of preparation not given.

EXPERIMENTAL

1. The oxidation of β-methylcyclohexanone

For 100 g of the ketone there were used 252 g of HNO_3 (sp. gr. 1.37), 80 ml of water, and 0.2 g of ammonium metavanadate (this gave 2.58 moles of HNO_3 per 1 mole of ketone). The reaction was carried out in a liter round-bottomed flask fitted with a dropping funnel and a reflux condenser. The mixture of nitric acid, water, and ammonium vanadate was heated to 90°, and 3 g of ketone first added. After a violent reaction began, the temperature of the bath was lowered to 60°, and the ketone dropped into the nitric acid at such a speed as to keep the reaction going not too violently. After all the ketone had been added, the mixture was heated for 1 hour on the boiling water bath, diluted with $^1/_3$ its volume of water, and allowed to stand overnight. In this way, a total of 1551 g of β-methylcyclohexanone was oxidized.

The strongly acid product obtained in different experiments was united, poured into a porcelain beaker and concentrated on the water bath in a hood, with water being added from time to time to help remove the excess of nitric acid. When this objective had been attained, the mixture in each beaker was evaporated until crystals appeared. After standing overnight in the cold, these were filtered off with suction and washed with ice water. The crystals were dried on filter paper; they melted at 85-89°. After the removal of the crystals, the filtrate and the wash water were united and again concentrated, but in this case it was already much more difficult to obtain good crystals. They were colored yellow and melted at 74-79°. The second filtrate, which had a syrupy character, was again diluted with water and concentrated. The crystalline slurry which formed was dried. It had a very low melting point (about 30°). The filtrate gave no crystals upon concentration, and it was treated in the following manner: It was treated with ether in an extraction funnel. During this process, a small amount of oxalic acid (m.p. 178°) separated out of the aqueous layer. The ether was driven off from the ether extract, the residue treated with alkali, and the neutral products removed from the alkaline solution with ether. After this the solution was acidified with mineral acid and the methyladipic acid was separated. In certain cases, the residue after the ether had been driven out was treated not with alkali, but with benzene in an extractor, and the benzene solution was made to precipitate the solute by the addition of two volumes of hexane. In both cases, a gruel-like mass was obtained. In some cases it stubbornly maintained its ointment-like character, but in others, pressing on a porous plate converted it into crystals with m.p. 62-67° (melting point of α-methyladipic acid 64°). In all, from 1551 g of β-methylcyclohexanone, there was obtained in this manner 1843.9 g of acids (83% of theory), although the different fraction, obtained by concentration, crystallization, etc., had different melting points and therefore contained different relative quantities of α- and β-methyladipic acids.

2. The ketonization of the mixture of methyladipic acids

The mixture of acids, in portions of 75 g, was subjected to slow distillation in the presence of barium hydroxide (0.01 mole of $Ba(OH)_2$ was used per 1.36 mole of acid) from a Wurtz flask of 250 ml capacity, at a flask temperature of from 250 to 295°. The yield of ketones fluctuated, depending on the properties of the sample of the acid mixture used, but the average consisted of about 50% of theory. The mixture of ketones obtained was distilled in the usual manner within the range 136-145°, and had n_D^{20} 1.4311-1.4343.

3. The action of the Grignard reagent on the mixture of ketones

a) The reaction with methyl iodide was carried out under the usual conditions:

in a three-necked flask fitted with a reflux condenser, stirrer, and dropping funnel. The magnesium and methyl iodide were used in slight excess with respect to the ketone. The decomposition of the reaction product was carried out, under cooling, first with water and then with dilute hydrochloric acid (1:5). The tertiary alcohols formed were not separated, but were dehydrated by distillation with iodine or crystalline oxalic acid. From 100 g of the ketone mixture there was obtained about 50 g of unsaturated hydrocarbons, which amounted to about 51% of the mixture of ketones used for the Grignard reaction. In another experiment, 60 g of ketones gave 31 g of the mixture of unsaturated hydrocarbons (52.7% of theory).

The unsaturated hydrocarbons were distilled in a column of 30 theoretical trays. Fig. 1 shows the results of the distillation of the unsaturated hydrocarbons obtained in two experiments. Curve I illustrates the composition of the hydrocarbons obtained from the mixture of acids with a high melting point (predominantly β-methyladipic acid), and Curve II is for the acids with low melting point (with a considerable content of α-methyladipic acid). On Curve I, the portion with b.p. 92.0-92.5° at 751 mm (n_D^{20} 1.4287, d_4^{20} 0.7720) corresponds to 2,4-dimethylcyclopentene-1 [7], and the portion with b.p. 104-104.5° at 751 mm (n_D^{20} 1.4444, d_4^{20} 0.7954) to 1,2-dimethylcyclopentene-1. The amounts of these fractions were in the ratio 6:1. In Curve II, these same hydrocarbons are reflected in the portions 91.5-92.7° at 750 mm and 103.1-104.6° at 750 mm, in relative quantities 1.4:1.0.

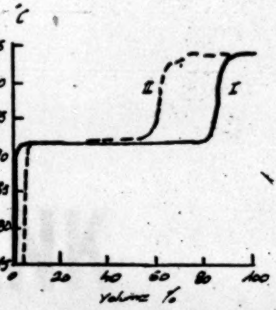


Fig. 1.

The 2,4-dimethylcyclopentene-1 obtained in both experiments was mixed and distilled once more in the same column. It all boiled at 92.7° at 750 mm and had n_D^{20}1.4287 and d_4^{20} 0.7715. When it was passed through platinized charcoal in a glass tube heated to 150° in a stream of hydrogen, it was converted into 1,3-dimethylcyclopentane with constants very close to those obtained by us for an earlier [7] preparation:

B.p. 90.6° at 750 mm; n_D^{20} 1.4096; d_4^{20} 0.7452; MR_D 32.56.
Found for C_7H_{14} 32.33 Aniline point 48.6°.

The fraction containing 1,2-dimethylcyclopentene-1 was also hydrogenated, but in alcoholic solution at room temperature in the presence of platinized carbon and chloroplatinic acid. The 1,2-dimethylcyclopentane obtained was distilled in a Vigret dephlegmator from 93.5 to 95.0° at 747 mm, and had:

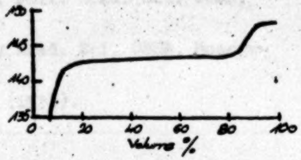
n_D^{20} 1.4163; d_4^{20} 0.7596; MR_D 32.43.
Computed for C_7H_{14} 32.33,

i.e., it contained about 60% of the trans-isomer and 40% of the cis-isomer.

According to the literature, trans-1,2-dimethylcyclopentane has b.p. 91.2-91.5° at 760 mm, n_D^{20} 1.4126, d_4^{20} 0.7520; cis-1,2-dimethylcyclopentane has b.p. 98.1-98.5° at 760 mm, n_D^{20} 1.4215, d_4^{20} 0.7719.

b) The reaction of the mixture of ketones with propylmagnesium bromide under the conditions previously described led to a mixture of tertiary alcohols which were not separated but immediately dehydrated by distillation with iodine. The washed and dried unsaturated hydrocarbons which were obtained were also distilled in a column of 30 plates. The distillation curve is given in Fig. 2. On it there are clearly visible horizontal portions with b.p. 143-143.8° at 732 mm (n_D^{20} 1.4405, d_4^{20} 0.7924), and 148.5° at 732 mm (n_D^{20} 1.4491, d_4^{20} 0.8062). The constants of the second fraction correspond to the 1-methyl-2-propylcyclopentene-1 of Chiurdoglou [8]:

B.p. 150.1-150.2° at 760 mm, n_D^{20} 1.4492, d_4^{20} 0.8059.



Because of the tiny amount obtained, it was not subjected to further treatment. The first fraction was hydrogenated in the vapor phase in the presence of platinized charcoal at 160°, and in alcoholic solution at ordinary temperature in the presence of platinized charcoal, a solution of H_2PtCl_6, and 10 ml of concentrated hydrochloric acid. In the first case after shaking with concentrated sulfuric acid and distillation from a Favorsky flask, 1-methyl-3-propylcyclopentane was obtained:

B.p. 147-147.8° at 752 mm, n_D^{20} 1.4246; d_4^{20} 0.7723.

The same hydrocarbon was obtained in the second case:

B.p. 147-147.8° at 752 mm, n_D^{20}1.4248; d_4^{20} 0.7728.

Thus, despite the different conditions of hydrogenation, no differences in the properties of the two preparations were observed. They were both united and distilled through the column. 1-Methyl-3-propylcyclopentane was obtained with the following constants:

B.p. 148.2-148.4° at 760 mm; n_D^{20} 1.4254; d_4^{20} 0.7715; MR_D 41.86.
Computed for C_9H_{18}: 41.56. Aniline point 57.8°.

SUMMARY

1. β-Methylcyclohexanone is oxidized by nitric acid in the presence of ammonium metavanadate to give a mixture of α-methyl and β-methyladipic acids, the second predominating.

2. The mixture of these acids may be subjected, without separation, to cyclization, the ketones obtained being used in the Grignard reaction with alkyl magnesium halides. The mixture of tertiary alcohols formed can split off water and be converted into a mixture of disubstituted unsaturated hydrocarbons. This mixture may, by distillation with a sufficiently effective column, be separated into the 1,2- and 1,3- disubstituted cyclopentenes and the latter converted by hydrogenation into the corresponding cyclopentane homologs.

3. Starting with β-methylcyclohexanone, this method has been used to synthesize 1,3-dimethylcyclopentane, 1,2-dimethylcyclopentane, and 1-methyl-3-propylcyclopentane.

In conclusion, we wish to utilize the occasion to express our thanks to M.I. Batuev and A.D.Matveeva for the optical investigation of 1-methyl-3-propylcyclopentane.

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A STUDY OF THE REACTION OF SULFUR WITH UNSATURATED COMPOUNDS

VI. THE SYNTHESIS OF ISOMERIC α-PHENYLTHIOTOLENES

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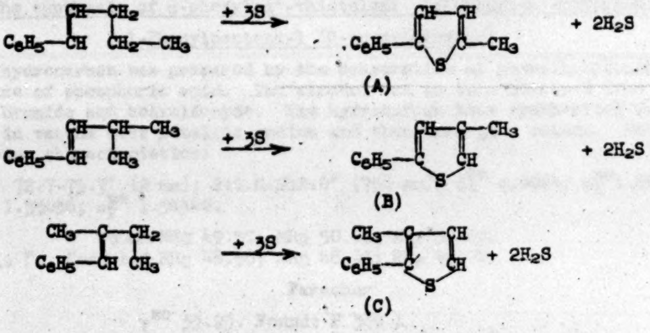
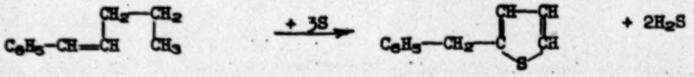
In previous communications [1-5] it has been shown that α- and β-phenyl thiophenes and their homologs are formed by the action of sulfur on phenyl substituted olefins and diolefins, and even on higher alkylbenzenes. In all cases, the thiophene ring is formed by means of an intramolecular closure of the aliphatic radical across the sulfur. There must be not less than four atoms of carbon in the form of a straight chain, without quaternary carbon atoms, and it makes no difference whether the chain contains double bonds, or how these are distributed.

The objective of the present communication is to report on the synthesis of all three isomers of α-phenylthiotolene (A, B, and C), two of which (B and C) have up to now been unknown. For this purpose we studied the reaction of sulfur with 1-phenylpentene-1, 3-methyl-1-phenylbutene-1, and 2-methyl-1-phenylbutene-1. As a result we obtained all the expected α-phenylthiotolenes in yields of 15, 20, and 18%, respectively, in accordance with the equations:



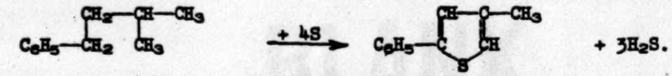
In the case of the reaction of 1-phenylpentene with sulfur, we may expect that along with the α-phenyl-α'-thiotolene (A), the formation of α-benzylthiophene may take place according to the equation:



C_6H_5—CH=CH CH_2—CH_2 CH_3
+ 3S
C_6H_5—CH_2—C CH—CH CH S
+ $2H_2S$

Both α-phenyl-α'-thiotolene and α-benzylthiophene are described in the literature. The first is in the form of white crystals with m.p. 49-51° and b.p. 270-272°, giving a blue-violet color [8] with isatinsulfuric acid. The second is a liquid with a pleasant fruity odor, boiling at 265°, and giving a red color with isatinsulfuric acid. The product obtained by us upon treating 1-phenylpentene-1 with sulfur was in the form of white crystals with m.p. 47.5-48.5° and b.p. 269-271°, giving a blue-violet color with isatinsulfuric acid. This definitely indicated that it was α-phenyl-α'-thiotolene and that during the reaction of sulfur with 1-phenylalkenes-1 containing a long chain, the formation of the thiophene ring takes place directly next to the aromatic nucleus. However, the possibility of another, secondary reaction must not be excluded, as along with the α-phenyl-α'-thiotolene, there was obtained a small amount (yield less than 1%) of a liquid with b.p. 260-265°, giving a blue color with isatinsulfuric acid. Apparently, this was α-benzylthiophene.

We have further shown that α-phenyl-β-thiotolene (B) can be smoothly obtained (yield up to 12%) by treating 2-methyl-4-phenylbutane (isoamylbenzene) with sulfur according to the equation:



C_6H_5—CH_2 CH_2—CH—CH_3 CH_3
+ 4S
C_6H_5—C CH—C—CH_3 CH S
+ $3H_2S$.

Finally, we attempted to make sulfur react with alkylbenzenes containing tertiary alkyl radicals. For this purpose, we boiled tertiary butylbenzene and tertiary amylbenzene with sulfur for 45 to 50 hours. However, except for the unchanged hydrocarbons, it was impossible to obtain any definite products of the reaction.

EXPERIMENTAL

I. The synthesis of α-phenyl-α'-thiotolene (α-phenyl-α'-methylthiophene)

1-Phenylpentene-1 (β-propylstyrene)

The hydrocarbon was prepared by the dehydration of phenylbutylcarbinol in the presence of phosphoric acid. The alcohol was in turn obtained from butylmagnesium bromide and benzaldehyde. The hydrocarbon thus synthesized was distilled twice in vacuum over metallic sodium and then through a column. It then had the following characteristics:

B.p. 72.7-73.7° (2 mm); 211.0-212.0° (758 mm); d_4^{20} 0.9024; n_C^{20} 1.52502; n_D^{20} 1.53036; n_F^{20} 1.54442.

Found MR_C 49.57; MR_D 50.01; MR_F 51.09.
$C_{11}H_{14}\Gamma_4$. Computed MR_C 48.58; MR_D 48.93; MR_F 49.72.

Parachor

γ^{20} 33.23. Found: P 389.1
Computed: P 391.1 (Sugden).
Data in Literature: Levy [8] B.p. 210-215°; n_D^{18} 1.5302.

The action of sulfur on 1-phenylpentene-1

In a flask fitted with a reflux condenser and a thermometer there were placed 27.8 g (0.19 mole) of 1-phenylpentene-1 and 18.3 g (0.57 g-atom) of sulfur. The mixture was heated on an air bath. The evolution of hydrogen sulfide began at 200°. The heating was continued for 27 hours at 210-235° until the evolution of hydrogen sulfide had completely ceased. The product of the reaction was a black tarry mass. This was extracted with boiling alcohol. The alcoholic solution was treated with metallic mercury and filtered. The alcohol was driven off and the residue fractionally distilled twice over powdered iron. Wide fractions with boiling range 260-269° were collected. The greater part crystallized (yield of crude crystals 5.0 g, or 15% of theory). These were recrystallized three times from alcohol. The crystals obtained were further purified by sublimation. Yield of pure substance 4.1 g, or 12.5% of the theoretical. The α-phenyl-α'-thiotolene obtained had the following characteristics:

M.p. 47.5-48.5°; b.p. 269-271° (762.5 mm).
0.0601 g substance: 17.95 g benzene; Δt 0.101°.
0.1060 g substance: 17.95 g benzene; Δt 0.181°.
Found: M 167.3, 170.0.
$C_{11}H_{10}S$. Computed: M 174.25.
0.2024 g substance: 0.2673 g $BaSO_4$.
0.2114 g substance: 0.2815 g $BaSO_4$.
Found %: S 18.13, 18.29.
$C_{11}H_{10}S$. Computed %: S 18.40.

Literature data for α-phenyl-α'-thiotolene: Paal [6] m.p. 49-51°; b.p. 270-272°.

The substance sublimed in the form of long white needles. With isatinsulfuric acid it gave a blue-violet color, with concentrated sulfuric acid, a yellow-orange color.

After recrystallization, there was obtained from the mother-liquor 0.25 g of liquid boiling at 260-265°. This gave an intense red color with isatinsulfuric acid.

II. The Synthesis of α-phenyl-β'-thiotolene (α-phenyl-β'-methylthiophene)

3-Methyl-1-phenylbutene-1 (β-isopropylstyrene)

The hydrocarbon was obtained by the dehydration of phenylisobutylcarbinol over molten sodium bisulfate. The carbinol was obtained from benzaldehyde and isobutylmagnesium chloride. The hydrocarbon thus synthesized was distilled twice through a column over metallic sodium.

B.p. 206.5° (767.7 mm); d_4^{20} 0.8907; n_C^{20} 1.52080; n_D^{20} 1.52621.
Found; MR_C 49.87; MR_D 50.32.
$C_{11}H_{14}S \lceil_4$. Computed: MR_C 48.58; MR_D 48.93.

Parachor

γ^{20} 31.40. Found: P 388.6.
Computed: P 391.1 (Sugden).

Literature data: Klages [8] b.p. 207° (757 mm); $d_4^{14.8}$ 0.8903; n_D^{20} 1.5248. Kunckell, Stahel [10] d_4^{14} 0.887; n_D^{20} 1.5251; Levy [8] b.p. 201-203°; d_4^{0} 0.9194; n_D^{18} 1.532.

The action of sulfur on 3-methyl-1-phenylbutene-1

49.2 g (0.32 mole) of hydrocarbon and 30.7 g (0.96 g-atom) of sulfur were heated in a flask fitted with a reflux condenser and a thermometer at 210-220° for 14 hours. The reaction product, a black tarry mass, was distilled in vacuum. The wide fraction boiling from 70 to 170° at 6 mm was collected. This was treated with mercury (in ether solution) and distilled twice over iron powder. The yield of pure α-phenyl-β'-thiotolene with b.p. 278-280.8° (773.5 mm) was 10.4 g, or 20.3% of the theoretical.

m.p. 17.3°; b.p. 280.0° (773.3 mm); d_4^{20} 1.1070.
n_C^{20} 1.62345; n_D^{20} 1.63216; n_F^{20} 1.65653.
Found: MR_C 56.48; MR_D 56.91; MR_F 57.85.
$C_{11}H_{10}S\lceil_5$. Computed: MR_C 53.62; MR_D 54.05; MR_F 55.04.

Parachor

γ^{20} 41.79. Found: P 400.2
Computed: P 402.6 (Sugden); 398.0 (Memford and Phillips); 399.4 (Gibling).
0.3388 g substance: 18.58 g benzene; Δt 0.550°.
0.2598 g substance; 13.90 g benzene; Δt 0.561°.
Found: M 170.1, 174.3.
$C_{11}H_{10}S$. Computed: M 174.25.
0.3691 g substance: 0.4881 g $BaSO_4$.
0.2434 g substance: 0.3195 g $BaSO_4$.
Found %: S 18.17, 18.03.
$C_{11}H_{10}S$. Computed %: S 18.40.

This substance was a colorless liquid with a characteristic odor. It solidified when cooled with snow. With isatinsulfuric acid it gave a characteristic indophenin reaction – a red-violet color.

2-Methyl-4-phenylbutane (isoamylbenzene)

Isoamylbenzene was obtained from bromobenzene, isoamyl bromide, and metallic sodium in boiling benzene medium. The hydrocarbon obtained was distilled twice in a column over metallic sodium.

B.p. 197.2° (755.6 mm); d_4^{20} 0.8542; n_C^{20} 1.48187; n_D^{20} 1.48572; n_F^{20} 1.49509.

Parachor

γ^{20} 28.34. Found: P 400.4
Computed: P 402.1 (Sugden).

Literature data: Klages [11] b.p. 198-199° (757 mm); $d_4^{15.6}$ 0.8625; $n_D^{15.6}$ 1.4867. Galpern [12] n_C^{20} 1.48207; n_D^{20} 1.48585; n_F^{20} 1.49534. Ipatiev [13] b.p. 197-199°; n_D^{20} 1.4835.

The action of sulfur on 2-methyl-4-phenylbutane

In a round-bottomed flask fitted with a reflux condenser and a thermometer, there were placed 35.8 g (0.24 mole) of isoamylbenzene and 30 g (0.96 g-atom) of sulfur. The reaction mixture was heated to boiling. Twenty minutes after boiling began, an evolution of hydrogen sulfide took place. The reaction was carried out for 14 hours at 200-245° until the evolution of hydrogen sulfide had completely ceased. The reaction product, in the form of a black, tarry mass, was extracted with boiling methyl alcohol. The alcohol was driven off and the residue subjected to fractional distillation above iron powder. This gave 5.4 g of a substance with b.p. 265-270° (yield 18%). After a second distillation over iron powder, 3.5 g of the pure compound was obtained (yield 8.5% of the theoretical):

M.p. 17.2°; b.p. 278.6° (764.7 mm); d_4^{20} 1.1069; n_C^{20} 1.62320; n_D^{20} 1.63196; n_F^{20} 1.65626. γ^{20} 41.76.

These values agree well with the values given above for α-phenyl-β'-thiotolene obtained from β-isopropylstyrene.

0.1005 g substance: 15.12 g benzene; Δt 0.198°.
0.1134 g substance: 16.18 g benzene: Δt 0.209°.
Found: M 172.1, 171.8.
$C_{11}H_{10}S$. Computed: M 174.25.
0.1562 g substance: 0.2074 g $BaSO_4$.
0.1297 g substance: 0.1725 g $BaSO_4$.
Found %: S 18.24, 18.31.
$C_{11}H_{10}S$. Computed %: S 18.40.

With isatinsulfuric acid it gave a characteristic red-violet color.

III. The synthesis of α-phenyl-β-thiotolene (α-phenyl-β-methylthiophene)

1-Phenyl-2-methylbutene-1 (β-methyl-β-ethylstyrene)

The hydrocarbon was obtained by the dehydration of methylethylbenzylcarbinol in the presence of traces of iodine. The alcohol was synthesized from benzylmagnesium chloride and methylethylketone. The hydrocarbon thus obtained was washed with a solution of alkali, dried over calcium chloride, and then twice distilled through a column over metallic sodium. The yield of hydrocarbon with b.p. 199-203° (759 mm) was 61.9% of the theoretical:

B.p. 202.0° (758.6 mm); d_4^{20} 0.8937; n_C^{20} 1.51724; n_D^{20} 1.52208; n_F^{20} 1.53473.

Found: MR_C 49.44; MR_D 49.81; MR_F 50.95.
$C_{11}H_{14}\Gamma_4$. Computed: MR_C 48.58; MR_D 48.93; MR_F 49.72.

Parachor

γ^{20} 31.80. Found: P 388.5.
Computed: P 391.1 (Sugden).

Literature data: Levy [14] b.p. 201-202°; d^0 0.924; n_D^{18} 1.528.
Tiffenault, Levy [15]. B.p. 199-200° (769 mm).

The action of sulfur on 1-phenyl-2-methylbutene-1

In a round-bottomed two-necked flask fitted with a reflux condenser and a thermometer, there were placed 180 g (1.2 mole) of the original hydrocarbon and 119.0 g (3.7 g-atom) of sulfur, The reaction mixture was heated at 210-220° for 12 hours. The reaction product was distilled in vacuum. The broad fraction collected, with boiling range 124-160° (7 mm) was washed with a solution of sodium plumbite to remove traces of mercaptans, then with water. It was then dried over calcium chloride. After 2 distillations through a column over iron powder, 25.1 g of pure α-phenyl-β-thiotolene (yield 11.6% of the theoretical) was obtained. B.p. 256.8-258.5° (764.7 mm).

B.p. 256.8-258.5° (764 mm); d_4^{20} 1.1067; n_C^{20} 1.60858; n_D^{20} 1.61584; n_F^{20} 1.63519.

Found: MR_C 55.76; MR_D 56.29; MR_F 57.70.
$C_{11}H_{10}S\,\Gamma_3$. Computed: MR_C 53.62; MR_D 54.06; MR_F 55.09.

Parachor

γ^{20} 39.09. Found: P 402.9.
Computed: P 402.6 (Sugden); 399.4 (Gibling).
0.1028 g substance: 14.42 g benzene: Δt 0.209°.
0.1482 g substance: 14.42 g benzene: Δt 0.306°.
Found: M 175.0, 172.3
$C_{11}H_{10}S$. Computed: M 174.25.
0.1111 g substance: 0.1486 g $BaSO_4$.
0.1996 g substance: 0.2658 g $BaSO_4$.
Found %: S 18.37, 18.29.
$C_{11}H_{10}S$. Computed %: S 18.40.

The α-phenyl-β-thiotolene obtained was in the form of a colorless liquid which gave a violet color with isatinsulfuric acid.

The action of sulfur on tertiary butylbenzene

The original hydrocarbon was obtained by alkylating benzene with isobutyl alcohol in the presence of sulfuric acid. The tertiary butylbenzene was distilled in a column over metallic sodium. It then had the following characteristics:

B.p. 167.5-168.2° (759.5 mm); d_4^{20} 0.8668; n_C^{20} 1.48832; n_D^{20} 1.49215; n_F^{20} 1.50212.

Parachor

γ^{20} 28.52. Found: P 357.8.
Computed: P 363.1 (Sugden).

26.8 g (0.2 mole) of the hydrocarbon and 32.1 g (1 g-atom) of sulfur were heated with a reflux condenser for 50 hours at 180-200°. No products of sulfuration were detected which were volatile at 1 mm. 6.5 g of the original tertiary butylbenzene remained unchanged. After 2 distillations over metallic sodium it had b.p. 166-168° (761.2 mm); d_4^{20} 0.8665; n_D^{20} 1.49212. The non-volatile tar which was formed in the reaction was not investigated more closely.

The action of sulfur on tertiary amylbenzene

The original hydrocarbon was obtained by the alkylation of benzene with isoamyl alcohol in the presence of sulfuric acid. After 2 distillations through a column over metallic sodium, it had the following characteristics:

B.p. 188.5° (751 mm); d_4^{20} 0.8679; n_C^{20} 1.49090; n_D^{20} 1.49468; n_F^{20} 1.50428.

Parachor

γ^{20} 29.02. Found: P 396.6.
Computed: P 402.1 (Sugden).

91.5 g (0.6 mole) of the hydrocarbon and 60.0 g (1.9 g-atom) of sulfur were heated in a flask fitted with a reflux condenser and a thermometer for 58 hours at 200°. Hardly any hydrogen sulfide was evolved. When the reaction product was distilled in vacuum, 70 g of unchanged tertiary amylbenzene was obtained. After 2 distillations in vacuum over sodium this had b.p. 190-190.5° (752.4 mm); d_4^{20} 0.8679; n_D^{20} 1.49496; γ^{20} 29.0. No products of sulfuration of any sort could be isolated from the reaction mixture.

SUMMARY

1. The reaction of sulfur with 3-methyl-1-phenylbutene-1, 2-methyl-1-phenylbutene-1, 1-phenylpentene-1, 2-methyl-4-phenylbutane, 2-methyl-2-phenylbutane, and 2-methyl-2-phenylpropane has been investigated.

2. The compounds α-phenyl-α'-thiotolene, α-phenyl-β-thiotolene, and α-phenyl-β'-thiotolene have been synthesized and described (the latter two have been unknown up to the present time).

3. It has been shown that tertiary butylbenzene and tertiary amylbenzene do not form any volatile sulfuration products even upon prolonged heating with sulfur at 200°.

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*See CB translation p. 1357 ff.

THE MECHANISM AND END PRODUCTS OF THE AUTOXIDATION OF RESIN ACIDS

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I

The oxidation of primary resin acids under natural conditions by the oxygen of the air has considerable technical significance. In the USSR these oxidized acids are obtained either from tar-impregnated stump wood by extraction with polar solvents or from resin which has seeped through an accidental wound of a fir (fir sweat). We may expect that our industry will obtain increasing quantities of oxidized resin acids.

It is impossible to handle them properly without knowing their chemical structure, their properties, and their ability to undergo chemical change. In these respects, only very little is known. It is known that almost all the primary (except for dextro-pimaric) and secondary resin acids (except for dehydro-, dihydro-, and tetrahydro-abietic) are easily oxidized by the oxygen of the air [1]; that during autoxidation, up to two atoms of oxygen can be added to a molecule of resin acid; that the oxidized resin acids are either insoluble in gasoline or soluble with difficulty, and that gasoline may therefore be used to separate them from unoxidized resin acids; that they are relatively stronger acids than when unoxidized, and are not precipitated from solutions of their alkaline salts by carbon dioxide.

At present it is known in general that the resins of different species of pines contain only three primary resin acids: dextropimaric (difficult to oxidize), laevopimaric, present in small quantities, and α-sapinic (chief part). That the same thing holds for fir resins has recently been shown by S.Malevskaya [2]. The velocity of oxidation of the two latter acids by air is approximately the same, and therefore the oxidized resin acids extracted from rosin and "fir sweat" must be chiefly derivatives of α-sapinic acid.

II

What is the mechanism of the oxidatinn of resin acids by the oxygen of the air? There is only the single investigation of M. and K. Pavlyuchenko [3] on this question. The authors believe that the molecules of oxygen add on to the double bond of the resin acids to form peroxides. This is indicated, in their opinion, by the lowering of the iodine number of the oxidation product, and by its tendency to release iodine from an acidified solution of potassium iodide. To us these conclusions do not seem too well justified. At the present time, the products of the autoxidation of unsaturated cyclic compounds, in particular the terpenes, have been comparatively thoroughly studied [4]; these include alcohols and ketones with unchanged double bonds and hydrocarbons with the skeleton of the original hydrocarbon, the entering atoms of oxygen being attached in the α-position to the double bond present, thrusting between the atoms of carbon and hydrogen. The primary products of autoxidation may be, according to the theory of Engler and Bakh, peroxides, which at the second stage give up half their oxygen to unoxidized molecules, with the formation of two molecules of oxide (Pavlyuchenko's mechanism) or two molecules of hydroxyl derivatives (our mechanism).

According to Pavlyuchenko's mechanism, the autoxidation of any resin acids must be represented thus:

$$C_{20}H_{30}O_2\cdot 2\,\Gamma + 2\,O_2 = C_{20}H_{30}O_2\cdot 2\,O_2;$$

$$C_{20}H_{30}O_2\cdot 2O_2 + 2C_{20}H_{30}O_2\cdot 2\Gamma = C_{20}H_{30}O_2\cdot 2\,O\ \text{(dioxide)} + $$
$$+\ 2C_{20}H_{30}O_2\cdot O\cdot\Gamma\ \text{(monoxide)}$$

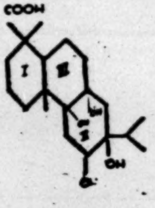
$$C_{20}H_{30}O_2\cdot 2O + 2H_2O = C_{20}H_{30}O_2\cdot 4OH = C_{20}H_{34}O_6\ \text{(saturated tetrahydroxy acid)}$$

$$C_{20}H_{30}O_2\cdot O\cdot\Gamma + H_2O = C_{20}H_{30}O_2\cdot 2\,OH\cdot\Gamma = C_2OH_{32}O_4\cdot\Gamma.$$
(unsaturated dihydroxy acid).

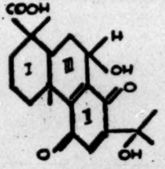
Thus, according to Pavlyuchenko's mechanism, the higher products of autoxidation of resin acids must contain the same amount (dihydroxides) of hydrogen as the original resin acid, or more, and must not contain double bonds, and the product must therefore be uncolored (absence of chromophore groupings).

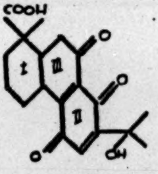
We consider it more probable that there is an analogy between the resin acids and the terpenes, and we expect that during autoxidation the entering atoms of oxygen will enter the α-position to the double bond present. How many such positions are there in the molecules of laevopimaric, α-sapinic, and abietic acids?

In all three cases, there are four such positions. Hence the composition of the above products of autoxidation of the resin acids will be either $C_{20}H_{30}O_6\cdot 2 =$ (unsaturated tetrahydroxy acid) or $C_{20}H_{26}O_6\cdot 2 =$ (oxidation of two secondary alcohol groups to ketone groups, or $C_{20}H_{24}O_6\cdot 2 =$ (oxidation of three secondary alcohol groups to ketone groups). In the two latter cases there can be chromophore groups; the p-quinone in the case of α-sapinic acid, and the e-diketodienoid in the case of laevopimaric acid and abietic acid. For α-sapinic acid, the chief component of the acid part of the resin, the end-products of autoxidation must have the following structure and compositions.



Pavlyuchenko's
mechanism
$C_{20}H_{34}O_6$





Our mechanism

$C_{20}H_{26}O_6$

$C_{20}H_{24}O_6$

According to both mechanisms, the phenomenon of autoxidation takes place in Rings II and III, and Ring I is untouched. However, it is not difficult to see that for α-sapinic acid, for example, the oxidation of the higher product of autoxidation with potassium permanganate will give, according to Pavlyuchenko's mechanism, the tribasic acid $C_{13}H_{20}O_6$, and according to our mechanism the acid $C_{12}H_{18}O_6$, which is known in the chemical literature [5]. According to Pavlyuchenko's mechanism, the molecule of the higher autoxidation product must contain no more nor less than the number of hydrogen atoms in the molecule of the original resin acid, must not contain double bonds, and must be uncolored. According to our mechanism it must keep two double bonds, must contain not more, but more likely fewer atoms of hydrogen than the molecule of the original resin acid, and in the latter case must be colored. The chromophore grouping of the main component of the higher stages of autoxidation of the acid portion of the resin must be the p-quinone, a fact which must be expressed correspondingly in the chemical behavior of this colored product.

III

To obtain highly oxidized products from the resin acids, we started with "fir sweat", as under the conditions of its formation (exudate on the trunk) it is already more oxidized than the resin from stump wood (stump in the ground). The acid portion of the exudate (cf. Experimental section) was separated on treatment with light gasoline into a gasoline-soluble and a gasoline-insoluble fraction. The latter fraction, on treatment with ethyl ether was separated into parts easily soluble and difficultly soluble in the ether. When the gasoline solution was allowed to stand, part of the weakly oxidized acids precipitated from it. We thus obtained: acids precipitated from gasoline solution (n.b.) 9.5% of the weight of sample; acids easily soluble in ether (e.s.e.) 34%; acids difficultly soluble in ether (d.s.e) 10%. N.b. and its solutions were colored pale yellow, while e.s.e. and d.s.e. and their solutions were colored dark red. These three fractions were studied, and the results of their analysis are given in Table 1.

TABLE

	n.b.	e.s.e.	d.s.e.
Formula closest to elementary composition	$C_{20}H_{30}O_3$	$C_{20}H_{26}O_5$	$C_{20}H_{26}O_6$
Data from combustion:			
% C	75.6, 75.6	69.9, 70.2	65.5, 65.9
% H	9.1, 9.0	7.4, 7.3	6.7, 6.8
Equivalents by alkali titration	317, 318	343	350
Number of double bonds (Kauffmann) [6]...	2.0, 2.1	2.2, 2.3	2.7, 2.7
Number of hydroxyl groups, including carboxyl (Tserevitinov), in dioxane	1.7, 1.8	2.5, 2.7	2.4, 2.7

According to all indications, these data confirm our mechanism of autoxidation and refute Pavlyuchenko's mechanism: 1) the composition of the higher products of autoxidation are expressed by the formulas $C_{20}H_{26}O_5$ and $C_{20}H_{26}O_6$, which correspond, according to our views, to the oxidation of two secondary hydroxyls to carbonyl groups; 2) these products are colored; 3) the double bond is retained in the products of autoxidation; 4) no more than two alcoholic hydroxyls are retained. (The determination of the number of hydroxyls was made considerably more difficult by the insolubility of these products in diisoamyl ether. It was necessary to experiment with a large number of solvents, the most suitable of which appeared to be dioxane, and in this the results are obviously too low because of the rapid formation of an insoluble precipitate of the magnesium salt of the oxidized resin acid, which reacts further with the excess of magnesium organic compound only very slowly. The results of the analysis of n.b., which without any doubt contains a single alcoholic hydroxyl, show that the unavoidable error is of the order of 0.2 per single alcoholic group).

These data permitted us to subject to confirmation the conclusions from our mechanism of autoxidation regarding the presence of the p-quinoid group in the main components of the oxidized resin acids of the composition $C_{20}H_{26}O_5$ and $C_{20}H_{26}O_6$ (see above). It is generally known that a large number of reducing agents (hydrogen sulfide, ammonium sulfide, hydrogen iodide, hydrogen at the moment of its evolution, sulfur dioxide, etc.) reduce colored quinone to a colorless hydroquinone. The latter can be oxidized back to the original quinone by a number of oxidizing agents (oxygen of the air, hydrogen peroxide, ferric chloride nitric acid, etc.).

Qualitative experiments on the reduction of the oxidized resin acids with the composition $C_{20}H_{26}O_5$ were carried out both in aqueous alkali and in acetic acid solution. In each case, the solution was divided into two parts; one half was subjected to reduction, the other served as a control. Under the action of the following reducing agents, the dark red color of the solution changed to light yellow: zinc dust in acetic acid upon heating; sulfurous acid in a sealed tube in acetic acid upon heating; hydrogen sulfide in alcoholic solution in a sealed tube quickly upon heating, slowly in the cold; ammonium sulfide in aqueous solution comparatively quickly without heating.

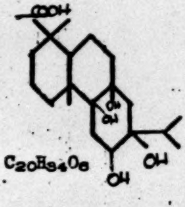
After the reducing agent had been removed, the reduced yellow solution quickly changed back to its original red color (comparison with control) when air was passed through it, and very quickly when a few drops of nitric acid were added to it. This reversible color reaction could be repeated any number of times, which makes it very probable that the quinoid grouping was present in our oxidized products.

An attempt was made to carry out a quantitative determination of the content of quinoid groups by titration of a reduced portion of the colored product with iodine [7] according to the equation:

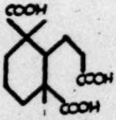
$$C_{20}H_{28}O_5 + I_2 = 2HI + C_{20}H_{26}O_5.$$

A number of analyses in good agreement gave the amount of iodine used up as 31.4 g per 100 g of sample, whence the content of quinone was calculated as 43%. The author of this method himself indicates that it is strictly applicable only for chemically pure compounds, whereas our mixture must doubtless contain not less than 35-40% [8] of the products of autoxidation of laevopimaric acid of the same composition, $C_{20}H_{26}O_5$, which does not possess a quinoid group (cf. above).

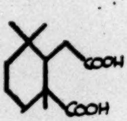
In accordance with the mechanisms of autoxidation of resin acids which we have considered, ours and Pavlyuchenko's, the first ring of the hydrophenanthrene skeleton is not affected by the oxidation, and must be preserved during the further energetic oxidation of the highly oxidized products with an aqueous solution of permanganate, but the composition and structure of the final products of oxidation must be different, as we can convince ourselves by considering the further oxidation of the higher products of autoxidation of α-sapinic acid:



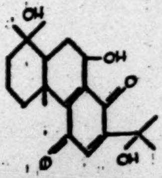
$C_{20}H_{34}O_6$



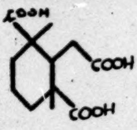
$C_{13}H_{20}O_6$
Main product
Pavlyuchenko's
mechanism



$C_{12}H_{18}O_6$
Byproduct

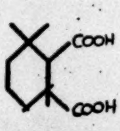


$C_{20}H_{26}O_6$



$C_{12}H_{18}O_6$

Main product
Our mechanism

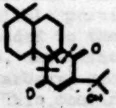


$C_{11}H_{16}O_6$

Byproduct

In order to confirm these conclusions experimentally, by the method described, we obtained a new sample of 'fir sweat", which had unfortunately been kept in the air in a thin layer an insufficient time to undergo additional autoxidation. The acids difficultly soluble in ether had the composition $C_{20}H_{25.3}O_{5.3}$, that is, they were somewhat less oxidized than the preceding sample had been. They were subjected to additional autoxidation. They were oxidized with 16 g-atoms of oxygen (rapid decolorization of $KMnO_4$ in the cold up to 12 g-atoms of oxygen, slow up to 16 g-atoms at 100°; with more, no $KMnO_4$ used up).

The volatile acids were removed by distillation with steam. Among them were found acetic and α-hydroxyisobutyric acid. The oxalic acid was separated from the non-volatile acids, which were then converted into the silver salts, whose silver content approached most closely to the formuls $C_{11}H_{13}O_6Ag_3$, and the silver salts were converted to the methyl esters. For the main fraction of the methyl esters, we found a saponification coefficient of 549. The requirement for $C_{11}H_{13}O_3(OCH_3)_3$ is 587; for $C_{12}H_{15}O_3(OCH_3)_3$, 560. The acids obtained by the saponification of the esters melted (different fractions) from 200 to 215°; $C_{11}H_{16}O_6$ melted at 219°, $C_{12}H_{18}O_6$ at 213°. An elementary analysis of these fractions gave figures which in the different cases approximated the composition of tricarboxylic acids with eleven, twelve, and thirteen carbons, but the fraction obtained in greatest quantity corresponded to the composition of the acid $C_{12}H_{18}O_6$. We explain the formation of the acid $C_{13}H_{20}O_6$ by the incorrectness of Pavlyuchenko's mechanism, and by the fact that the products of autoxidation used were not at the highest stage of oxidation ($C_{20}H_{25.3}O_{5.3}$ instead of $C_{20}H_{26}O_6$) and contained an acid of the structure:



which gave, upon further oxidation, the acid $C_{13}H_{20}O_6$.

The data given completely confirm the latter consequence of our mechanism of autoxidation of resin acids – the fact that the oxidative process does not affect the first ring of their hydrophenanthrene skeleton.

IV

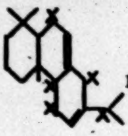
Resin and individual primary and secondary resin acids, when they are kept as powders or as thin layers in the air, absorb oxygen, and lose their solubility in gasoline. However, during this proces the color remains almost unaltered, and consequently no chromophore groups are formed.

The resin from stump wood and "fir sweat" is subjected to autoxidation in the presence of terpenes, atmospheric and soil moisture, and microflora (bacteria and fungi). It is known that peroxides act as dehydrogenating agents, and terpene peroxides may act in this way. A number of biochemical processes caused by bacteria and fungi are combinations of dehydrogenation and hydrogenation. These hydrogenations, which can take place during the autoxidation of the resin from stump wood and "fir sweat" under natural conditions, also lead to the formation of colored oxidized acids of the composition $C_{20}H_{26}O_5$ and $C_{20}H_{26}O_6$, starting from weakly colored acids of the composition $C_{20}H_{30}O_5$ and $C_{20}H_{30}O_6$.

During the autoxidation of dry resin and individual resin acids in the dry air of the laboratory in the absence of terpenes and under conditions that make it difficult for bacteria and fungi to be biologically active (absence of water) these dehydrogenation reactions cannot take place. Hence, if our mechanism for the autoxidation of resin acids is correct, the highest product of autoxidation must be an acid with the composition $C_{20}H_{26}O_2(OH)_4 = C_{20}H_{30}O_6$. In order to confirm these conclusions, we investigated the products of the autoxidation of abietic and α-sapinic acids.

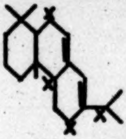
Two structural formulas have been proposed for abietic acid, by Krestinsky, and by Fieser:

a)



Krestinsky

b)



Fieser

Each author proposes his variant on the basis of a study of the products of ozonolysis of abietic acid. V.N.Krestinsky has shown that the results of ozonation lead with equal probability to both variants of structure, a and b, but he has preferred variant a on the basis of what seems to him a low exaltation of the molecular refraction (0.7) of the methyl ester of abietic acid. Later, Fieser gave spectrochemical evidence for structure b. To us variant b appears more probable. The small crosses designate free α-positions with respect to the double bond, accessible to autoxidation. In formula a there are five such positions, in formula b, four.

Abietic acid, ground to a powder, was kept in the air of the laboratory for one year and for five years. Both samples were extracted for a long time with light gasoline in order to remove the soluble portions, and the residues were investigated. Their compositions corresponded to the formula $C_{20}H_{30}O_6$. The compound contained four alcoholic hydroxyls, determined by acetylation. As this method does not affect the hydroxyl of the carboxyl group, the formula of the compound can be broken down to $C_{19}H_{25}(OH)_4COOH$. This confirms the previous considerations on the autoxidation of resin acids in the absence of moisture, terpenes, fungi, and bacteria.

Similar results have also been obtained in studying small samples of α-sapinic acid, kept uncrushed for not more than half a year in an apparatus which was first sealed, then accidentally broken, the accident not being noted at the time it happened. The residue insoluble in gasoline had the composition $C_{20}H_{30}O_5$. The smaller number of oxygen atoms in comparison with the preceding case is explained by the shorter period of storage and the uncrushed condition, and the lesser velocity of autoxidation of α-sapinic acid in comparison with abietic [1]. Both in this case, and in the preceding, autoxidation takes place without a change in the number of hydrogen atoms in the molecule of resin acid. In both cases, the higher products of autoxidation have a pale yellow color, as do their solutions.

These preliminary results on the composition of the higher products of the autoxidation of α-sapinic acid and abietic acid in the absence of terpenes, moisture, and fungi also correspond to our mechanism, and do not agree with Pavlyuchenko's mechanism.

EXPERIMENTAL

Fir sweat (700 g) was crushed to a powder and spread in a thin layer to be oxidized by the oxygen of the air for a week. It was then heated to the boiling point with 1500 ml of gasoline (b.p. below 100°). 299 g did not dissolve. Upon standing, a precipitate which weighed 57 g separated from the gasoline solution. This was filtered with suction. The mother liquor was diluted twice with gasoline, and 48 additional g of precipitate formed. Both precipitates were united (105 g) and shaken with a warm solution of 20 g of caustic soda in 200 ml of water. The solution was cooled and extracted four times with ether to remove neutral compounds. The ether was driven off from the ether extract. 26 g of neutral compounds were obtained. The alkaline aqueous solution was acidified with acetic acid and extracted with ether five times. The ether extract was washed with water three times, and the residue dried to constant weight (n.b. 65 g). Loss 14 g.

The 299 g of residue insoluble during the first heating with gasoline was extracted four times with alcohol (80 ml portions); 212 g dissolved, and ether extracted 18 g from what was left. The final residue contained 40 g. The alcoholic solution was treated three times with hot water to remove the alcohol and water-soluble compounds. The residue was dissolved in a small excess of aqueous ten percent alkali, and the solution extracted with ether five times. The ether extract was washed with alkali and then three times with water, and the ether driven off. There was 24 g of neutral compounds. The aqueous alkaline solution was acidified with acetic acid and extracted with ether five times. The ether was driven off from the extract. The acids soluble in ether amounted to 113 g (e.s.e.). The portion insoluble in ether was shaken with 10 ml of alcohol, 20 ml of 5% acetic acid (in order to decompose acid salts possibly present) and 20 ml of saturated NaCl solution, and then extracted with ether five times. The extract was washed with water and the ether driven off. The 21 g of acid obtained was added to that previously obtained (21 + 113 = 134 g).

The residue insoluble in ether was carefully washed with water and dried. Weight 53 g (d.s.e.). This 53 g was dissolved in 50 ml of alcohol and 420 g of ether was added to the solution. 5 g of a black powder precipitated. All the ether was driven off from the mother liquor, and half of the alcohol; the residue was again mixed with 420 g of ether, and 5 g of a lighter-colored substance precipitated. The solvent was driven off and the residue dried. It weighed 42 g.

In the investigation of the part of the fir sweat soluble in gasoline, it appeared that it contained saponifiable substances in very considerable amount. These substances, first removed from unoxidized resin acids, were saponified by boiling with alcoholic alkali. The alkaline solution gave acids which were separated according to the scheme described above, and corresponding fractions were united in the manner given above. In all there were obtained: n.b. 66 g; e.s.e 143 g; d.s.e 61 g. The results of the analyses are given above.

The determination of the number of hydroxyl groups in oxidized resin acids (Tserevitinov)

All the fractions of the acids were almost or completely insoluble in diisoamyl ether, and some were soluble only with difficulty in ethyl ether as well. It was necessary to seek a solvent that would be more suitable for this purpose. The single one suitable for all fractions appeared to be dioxane. It was purified by long boiling with sodium until there was no further reaction with the latter, and then distilled. It was impossible to obtain a Grignard reagent directly in the dioxane. A roundabout method was adopted. The ether solution of methylmagnesium iodide was poured into the dioxane, and the ether removed by means of the suction of a water-jet pump. The suitability of the solution obtained for determining the number of hydroxyl groups by Tserevitinov's method was tested with borneol and found acceptable. For the fractions of acid, we found:

	Sample (g)	Methane (ml)	Number of OH groups
n.b.	0.0546	6.55	1.71
$C_{20}H_{30}O_3$	0.0640	7.95	1.77
e.s.e.	0.0447	7.10	2.46
$C_{20}H_{26}O_5$	0.0581	10.10	2.67
d.s.e	0.0858	14.25	2.67
$C_{20}H_{26}O_6$	0.0775	11.45	2.40

Qualitative experiments on the reduction of colored solutions of e.s.e.

1. The red solution in glacial acetic acid was heated on a boiling water bath, and small portions of zinc dust were sprinkled in. As the zinc dissolved, the color of the solution changed to pale yellow.

2. The red solution in 98% acetic acid was saturated with sulfur dioxide. After four hours of heating in a sealed tube at 100°, the color of the solution had changed to pale yellow.

3. The red alcoholic solution was saturated with hydrogen sulfide. The fading of the color was notable even in the cold. The solution was sealed off, and the color changed quickly to pale yellow upon heating on a boiling water bath. The solution was decolorized even more quickly by a solution of ammonium sulfide.

The yellow solutions obtained resumed their original red colors (comparison with control) when air was passed through them for from two to six hours. The same thing happened quickly when a few drops of nitric acid was added.

The quantitative determination of the quinoid grouping in e.s.e with the composition $C_{20}H_{26}O_5$

A sample of e.s.e was reduced with zinc dust in acetic acid as described above. The excess of zinc was filtered off and washed. The filtrate was neutralized with caustic soda, using phenolphthalein, and titrated with iodine in the presence of starch. Seven determinations gave the amount of iodine used up per 100 g of e.s.e.: 31.6, 20.0, 32.2, 31.3, 32.2, 31.6, and 31.8; average 31.4 g. The equation

$$C_{20}H_{28}O_5 + I_2 = 2HI + C_{20}H_{26}O_5$$

leads to a computed result of 73.4 g.

The oxidation of $C_{20}H_{26}O_5$ from e.s.e. by a solution of potassium permanganate

60 g of e.s.e. was dissolved in 700 ml of 1% caustic soda solution and small amounts of $KMnO_4$ solution containing 73 g of salt per liter were added with stirring.

When 12 g-atoms of oxygen had been added, the rate of decolorization of the solution showed a sharp drop. It was necessary to heat the flask first to 55° and then on the boiling water bath. After sixteen g-atoms of oxygen had been absorbed, the decolorization of the permanganate ceased even at 100°. The excess of permanganate was destroyed with hydrogen peroxide, the manganese dioxide was filtered off with suction and washed several times with hot water, and the filtrate and wash water were evaporated to dryness. The dry residue was extracted with boiling methyl alcohol and the alcohol driven off from the extract. The dry potassium salts of organic acids amounted to 49 g. They were dissolved in water, acidified with hydrochloric acid using Congo red, and distilled with steam until the last portion of distillate was neutral. The entire distillate was neutralized and evaporated to a small volume, then made acid to Congo red, extracted with ether, and the extract distilled.

There were obtained: acetic acid, with b.p. 60-62° at 105 mm, coefficient of neutralization found 926, computed 933; hydroxyisobutyric, b.p. 63-65° at 7.5 mm, coefficient of neutralization 528, computed 539; m.p. 44-45°.

The acids non-volatile with steam which remained in the flask were extracted with ether for seven days in a continuous extractor. The ether was driven off, the acids neutralized with normal alkali, and the solution of salts precipitated with an amount of silver nitrate calculated from the amount of alkali used up. The silver nitrate solution was added in three portions. Three silver salt fractions were obtained. They analyzed:

		% H	% C	% Ag
Computed:	$C_{11}H_{13}O_6Ag_3$	2.3	23.2	57.3
	$C_{12}H_{15}O_6Ag_3$	2.6	24.8	55.9
Found:	1st fraction	1.5	20.0	59.4
	2nd fraction	1.6	20.6	59.0
	3rd fraction	1.7	21.4	57.5

These siver salts doubtless contained silver oxalate, which resulted in a lowering of their carbon and hydrogen content and an increase of the silver. The water solution was extracted with ether, and calcium chloride in acetic acid solution used to precipitate the oxalate (ca found 26.9%, calculated 27.3%) in an amount corresponding to 5 g of oxalic acid.

The silver salts (all three fractions) were converted into the methyl esters by heating with methyl iodide in benzene solution. The silver iodide was filtered off with suction, the benzene driven off, and the residue distilled in vacuum. The main fraction boiled at 135-160° at 0.6 mm pressure.

The saponification number was found to be 549. Calculated for $C_{11}H_{13}O_3(OCH_3)_3$ 587, for $C_{12}H_{15}O_3(OCH_3)_3$ - 560.

The main triester fraction was saponified by boiling for four hours with an excess of alcoholic alkali and then ten hours more after the solution had been diluted with an equal volume of water. The alcohol was driven off and the residue acidified to Congo red and extracted with ether. The ether was driven off from the extract. The residue began to crystallize after long standing. The oil was washed off from the crystals with a small quantity of ether. The crystals contained sodium, i.e., they were adulterated with an acid salt. They were again dissolved in water, acidified to Congo red with hydrochloric acid, and extracted with ether. After the ether had been removed, the residue did not completely crystallize (see below, "acid from acid salts"). The ether solution of the oil washed off from the acid salts gave an ointment-like precipitate, easily soluble in acetone. The ether was driven off from the mother liquor; the residue did not crystallize completely. Small samples of these precipitates ("acids from acid salts", "acids from acetone solution", "acids from ether solution") were freed from oil by smearing on a porous plate. They then melted at temperatures between 198 and 215°.

Analyses were carried out on the acids which were not squeezed on a porous plate but merely dried to constant weight:

		% H	% C
Computed	$C_{11}H_{16}O_6$	6.6	54.1
	$C_{12}H_{18}O_6$	7.1	55.8
Found	Acid from ether solution	7.2	56.9
		7.2	57.9
		7.1	58.2
	Acid from acetone solution	6.5	54.0
		7.0	53.9
	Acid from acid salts	6.5	55.6
		6.6	55.6
		6.7	55.9

The autoxidation of abietic acid

Abietic acid with m.p. 171-173° and $[\alpha]_D$ -87° was ground to a powder and sprinkled in a fine layer, then kept in the laboratory with access of air and light for one year and five years. By the methods described above, both samples gave a more oxidized portion which was yellow and hard. An elementary analysis of both samples gave approximately the same composition, corresponding to the absorption by a molecule of abietic acid of four atoms of oxygen.

	% C	% H
Sample that had stood for a year	64.9 64.9	8.2 8.3
Sample that had stood five years	65.6	8.4
Required for $C_{20}H_{30}O_6$	65.6	8.2

For the latter sample, the % H, by Tserevitinov's method, in amyl ether, was found equal to 12.9 and 13.6; found by acetylation, 18.4.

Required for $C_{20}H_{27}O_3(OH)_3$	13.9
Required for $C_{20}H_{26}O_2(OH)_4$	18.6
Molecular weight (Rast)	361
Required for $C_{20}H_{30}O_6$	366

Acid number found 161 and 162; required for $C_{20}H_{30}O_5$ 153.

The autoxidation of α-sapinic acid

α-Sapinic acid with m.p. 143-145° and $[\alpha]_D$ -60.3° was kept in a sealed tube in the form of crystals. The test tube was accidentally broken, and lay in this condition for not more than half a year. The contents were treated in the manner described. No products difficultly soluble in ether were found. The fraction insoluble in benzene and easily soluble in ether was analyzed. After the sample had been dried at 80° at a pressure of 10^{-3} mm, there was found:

% C 68.4 and 68.4; % H 8.4 and 8.0. Computed for $C_{20}H_{30}O_5$ C 68.5 %; H 8.6 %. Coefficient of neutralization found 358, 357, and 358; computed 350.

SUMMARY

1. A method has been found by which the oxidized resin acids can be separated into fractions of different degrees of oxidation.

2. A mechanism has been proposed for the autoxidation of resin acids. It leads to the penetration of oxygen atoms between the carbons and hydrogens in positions α to the double bond, with the formation of hydroxyl groups.

There are four such positions in primary resin acids and in abietic acid, and in accordance with this, the composition of the higher products of oxidation must be expressed by the formula $C_{20}H_{30}O_6$, which has also been found for the higher product of autoxidation of abietic acid under laboratory conditions. It contains four alcoholic hydroxyls.

3. The higher products of autoxidation of the primary resin acids under natural conditions have the composition $C_{20}H_{26}O_6$, and are deeply colored. In accordance with our mechanism, this is the result of the oxidation of two alcoholic hydroxyls to carbonyls, with the formation, in the case of α-sapinic acid (the main component of the acid portion of the resin) of a p-quinone grouping. It has been found that the products of autoxidation retain the double bonds of the original

resin acids and have two alcoholic hydroxyls.

4. It has been determined experimentally that under natural conditions, there is a high degree of probability that the quinone grouping is present in the higher products of autoxidation of primary resin acids.

5. All the results found experimentally agree with our mechanism and oppose the mechanism of Pavlyuchenko (the addition of oxygen to the double bond).

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* See CB translation p.1037 ff.

THE ACTION OF NITROGEN PEROXIDE ON THE ETHYL ESTER OF CINNAMIC ACID

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In a paper on "The Action of Nitrogen Peroxide on Cinnamic Acid" by one of the present authors, it was shown that the action of gaseous nitrogen peroxide on this acid gives a liquid addition product in which the nitrogen is attached to a carbon atom in the manner of a pseudonitrosite. The action of liquid nitrogen peroxide on cinnamic acid gave liquid and crystalline addition products. The addition products were reduced to give the corresponding aminoacids. Experiments with unsaturated hydrocarbons of the ethylene series showed that the composition of addition products of nitrogen oxides and the character of the bases obtained by their reduction differed, depending on the structure of the original compound.

It was of interest to explain the influence of substitutents attached to the carboxyl group of cinnamic acid on the formation of addition products with nitrogen peroxide. In particular, we were interested in the question of what sort of addition products would be formed by the action of nitrogen peroxide on the ethyl ester of cinnamic acid. Except for the work of I.V.Egorov [1] we have come across no results in the literature on the action of nitrogen oxides on the esters of unsaturated acids.

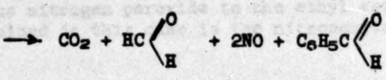
The ethyl ester of cinnamic acid was obtained by heating a solution of the acid in absolute alcohol in the presence of concentrated sulfuric acid. The ester obtained was a colorless liquid, soluble in organic solvents. The ester used for the reaction had: b.p. 269-270°; d_{15}^{15} 1.047; n_D^{20} 1.6002.

Gaseous and liquid nitrogen peroxide were allowed to act on the ethyl ester of cinnamic acid in a solution of dry ether under identical conditions. The action of gaseous nitrogen peroxide gave a liquid addition product and a crystalline substance. The liquid product lost nitrogen in the form of oxide upon standing, and upon long storage assumed the consistency of a viscous, smearable ointment. The moisture of the air hastened the increase of viscosity of the addition product; the addition of a small amount of hydroquinone inhibited the increase of viscosity of the liquid product of the addition of N_2O_4.

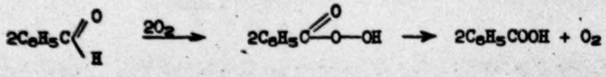
We encountered no explanation of this transformation in the literature. On the basis of our experiments, we are inclined to explain this phenomenon by the following mechanisms:

$$1)\ C_6H_5CHN_2O_4CHCOOC_2H_5 \xrightarrow{H_2O} C_2H_5OH + 2HNO_2 + C_6H_5CH{=}CH_2 + CO_2.$$

$$2)\ C_6H_5CHN_2O_4CHCOOC_2H_5 \xrightarrow{H_2O} C_2H_5OH + C_6H_5CHN_2O_4CHCOOH \longrightarrow$$



$$\longrightarrow CO_2 + HC\genfrac{}{}{0pt}{}{O}{H} + 2NO + C_6H_5C\genfrac{}{}{0pt}{}{O}{H}$$



$$2C_6H_5C{\overset{O}{\underset{H}{\lt}}} \xrightarrow{2O_2} 2C_6H_5C(=O)—O—OH \rightarrow 2C_6H_5COOH + O_2$$

However: 1) The failure to add halogen during the determination of the iodine number indicated the absence of compounds with ethylene bonds (styrene and its monomer);

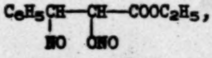
2) The failure of a precipitate to form upon the addition of methyl alcohol to a benzene solution of the product indicated the absence of styrene polymers;

3) When the product was stored in a desiccator, gases with a sharp odor, producing tears, were evolved;

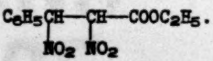
4) Benzaldehyde and crystals of benzoic acid were detected.

All this made the second mechanism seem more probable. In this mechanism, the benzoyl derivative of hydrogen peroxide is reduced to benzoic acid, and the oxygen given off again reacts with benzaldehyde. The result is the formation of a mixture of compounds, which lends a viscous consistency to the addition product of nitrogen peroxide to the ethyl ester of cinnamic acid. The second mechanism also makes comprehensible the influence of the hydroquinone on the inhibition of the increase of viscosity of the liquid addition product of N_2O_4, as it retards the oxidation of the benzaldehyde.

On the basis of these investigations, we characterized the liquid addition product of nitrogen peroxide to the ethyl ester of cinnamic acids as a mixture which consisted of the addition products of NO_2–ONO and NO_2–NO_2, i.e., as the nitronitrous ester I, and the dinitro compound II.

I. 

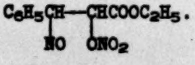
$$C_6H_5\underset{NO}{CH}—\underset{ONO}{CH}—COOC_2H_5,$$

II. 

$$C_6H_5\underset{NO_2}{CH}—\underset{NO_2}{CH}—COOC_2H_5.$$

Reduction of the liquid addition product with tin and hydrochloric acid gave a mixture of hydroxyamino- and diamino- acids.

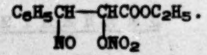
The crystalline addition product was in the form of beveled platelets, and had a blue color. The blue color was maintained when the substance was melted or dissolved in ethyl acetate. Upon standing in a desiccator over sulfuric acid, the substance was decolorized. On the basis of the results of our investigations, and of a comparison with the compounds previously obtained, we assumed the crystalline addition product to be the nitrosate or nitrosonitric ester:



$$C_6H_5\underset{NO}{CH}—\underset{ONO_2}{CH}COOC_2H_5.$$

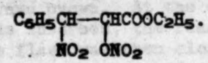
The action of liquid nitrogen peroxide on the ethyl ester of cinnamic acid gave a liquid product and two crystalline products. The liquid product, judging from the results of tests and its properties as a whole, seemed identical with the liquid addition product of gaseous nitrogen peroxide, that is, it was a mixture of the nitronitrous ester and a dinitro compound.

The crystalline addition products had different properties. The first had a blue color which disappeared upon standing, and melted at 131-132° to give a blue liquid, which decomposed with the formation of brown vapors at 162°. The beveled platelets dissolved in 50% alcohol and in ethyl acetate, coloring the acetate solution blue. The properties and results of analysis of this compound correspond to the properties and results of analysis of the crystalline addition product of gaseous nitrogen peroxide to the ethyl ester of cinnamic acid, i.e., the compound obtained in this case is the nitrosonitrate:



$$C_6H_5\underset{NO}{CH}-\underset{ONO_2}{CH}COOC_2H_5.$$

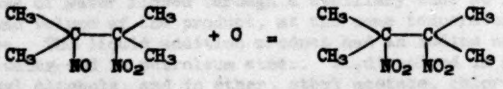
The second crystalline substance was in the form of colorless prismatic crystals, which melted at 151-152° to give a colorless liquid. This compound did not dissolve in 50% alcohol. It dissolved well in ethyl acetate, but did not color the acetate solution blue. On the basis of the results of investigation of this crystalline substance, we took it to be the nitronitrate of the ethyl ester of cinnamic acid:



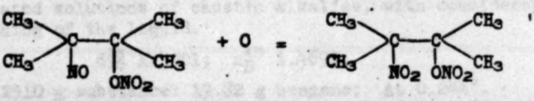
$$C_6H_5\underset{NO_2}{CH}-\underset{ONO_2}{CH}COOC_2H_5.$$

Thus, the action of gaseous, as well as of liquid nitrogen peroxide on the ethyl ester of cinnamic acid gave us, in addition to other addition products, a blue nitrosonitrate in both cases. There are data in the literature on the structure of similar products, and on the causes of their blue color.

Yu.Schmidt [2], N.Adkins [4], and Acad. N.Ya.Demyanov and K.V.Sidorenko [3] in their papers pay attention to the color of the products of reaction of nitrogen oxides with unsaturated hydrocarbons of the ethylene series, and consider this to be a physical sign of compounds which contain a nitro group. But the product with a blue color was not obtained in pure form, and the conclusions about it were drawn from the final products formed. In his work [5] "On the Reaction Between Nitric Anhdyride and Unsaturated Hydrocarbons of the Ethylene Series", Acad. N.Ya.Demyanov observes: "...as for the structure of the blue product, in view of the fact that it was not isolated, we can only guess. It might be either $C_6H_{12}N_2O_3$, i.e., a pseudonitrosite of tetramethylethylene, which is further transformed into a dinitro compound:



or it might be a nitrosonitrate, i.e., a tertiary nitrosate, which forms the nitronitrate:



''

In our previous work [6] we indicated the formation of two crystalline addition products of N_2O_4 to petroselinic acid, but we could not then spare the time to elucidate the causes for the formation of two products which differed in their properties.

In this case, on the basis of the experiments described below, we can say with assurance that the blue color of the addition product of N_2O_4 to the ethyl ester of cinnamic acid is determined by the presence of the nitroso group in the molecule. When this is oxidized to the nitro group, the product loses its color. The blue compound has been isolated and investigated. It is a nitrosonitrate, which goes over to the nitronitrate:

$$C_6H_5\underset{NO}{CH}-\underset{ONO_2}{CH}COOC_2H_5 + O = C_6H_5\underset{NO_2}{CH}-\underset{ONO_2}{CH}COOC_2H_5,$$

i.e., an addition product of N_2O_5 is formed.

EXPERIMENTAL

1. The action of gaseous nitrogen peroxide on the ethyl ester of cinnamic acid

A solution of 36.0 g of the ethyl ester of cinnamic acid in 75.0 ml of dry ether was saturated at 0° with nitrogen peroxide. In 10 hours, 64.0 g of N_2O_4 were absorbed. As the stream of N_2O_4 was passed through, the solution turned a pale yellow color, and then gradually turned brown. At the end, the saturated solution was dark brown. When no more gas was absorbed, the reaction mixture was allowed to stand for 2 hours in ice water. The flask was then closed with a stopper containing a tube filled with pieces of calcium nitrate, and allowed to stand overnight in a hood. On the following day the solution was filtered off and transferred to an evaporation dish in order to remove the solvent and the excess of nitrogen peroxide. The solvent and the excess N_2O_4 were removed by passing a stream of dry air through a porcelain desiccator which was cooled from outside. The removal of the solvent and the excess N_2O_4 gave 54.6 g of an oily addition product. The increase in weight of 18.6 g almost coincided with the amount calculated theoretically (19.4 g), assuming the addition of two NO_2 groups to the double bond of the side chain of ethyl cinnamate. Upon standing in a desiccator over sulfuric acid, the addition product formed crystals. The mixture of crystals was chilled and filtered. This gave 49.3 g of liquid addition product and 4.5 g of crystalline product impregnated with a brown tarry material.

Investigation of the liquid addition product of N_2O_4 to ethyl cinnamate

This compound was an amber-yellow oil considerably thicker and more viscous than water. The following experiment will give some idea of the viscosity of the product: a given volume of water flowed through a capillary tube at 17° in 3.6 seconds, while the same volume of the product, at the same temperature, flowed through in 112 minutes. The liquid addition product had an iodine number of zero, and was insoluble in water and in petroleum ether. It dissolved in methyl, ethyl, propyl, butyl, and amyl alcohols, and in ether, ethyl acetate, chloroform, acetone, benzene, and carbon tetrachloride. When it was boiled with water, the liquid turned brown, at the same time developing an acid reaction to litmus. The product dissolved in concentrated solutions of caustic alkalies, with considerable evolution of heat and frothing of the liquid.

d_{15}^{15} 1.3001; n_D^{45} 1.4692.

0.2510 g substance: 19.82 g benzene: Δt 0.244°.
0.3105 g substance: 19.82 g benzene: Δt 0.304°.
Found: M 259.5, 257.7.
$C_{12}H_{12}O_6N_2$. Computed: M 268.

4.203 mg substance: 7.690 mg CO_2; 1.826 mg H_2O.
3.411 mg substance: 6.229 mg CO_2; 1.478 mg H_2O.
6.011 mg substance: 0.576 ml N_2 (21.5°, 736 mm).
6.207 mg substance: 0.582 ml N_2 (18°, 738 mm).
Found %: C 49.92, 49.83; H 5.42, 5.50; N 10.76 10.68.
$C_{12}H_{12}O_6N_2$. Computed %: C 49.25; H 4.47; N 10.45.

Upon standing the addition product thickened and lost nitrogen in oxide form. Gases with a sharp odor and lachrymatory properties were evolved. A test made with starch-iodide paper to detect nitrous acid which had split off gave a positive result. The instability of the product was also confirmed by this experiment; a small amount of the material was placed in a test tube which was closed with a rubber stopper through the opening of which a glass tube was inserted the end of the tube being drawn into a capillary and bent over. The tip of the capillary was dipped into a beaker filled with water. The gas formed by the decomposition of the product pushed the water out of the capillary.

The instability of the product resulted in its becoming more viscous. The moisture of the air hastened the thickening process, as was confirmed by the following experiment. The liquid addition product was allowed to stand in two test tubes for 9 months. One test tube was closed with a cork stopper with fine perforations, the second was sealed with a rubber stopper containing a tube filled with calcined calcium nitrate. In the first tube the substance assumed the appearance of a viscous ointment, while on the walls of the test tube colorless needlelike crystals separated. These could not be isolated from the mixture. In the second test tube, the substance was almost unchanged. If a small amount of hydroquinone is added to the substance, the process of thickening takes place more slowly.

In order to explain the character and the stability of the nitrogen bonds in the addition product, the following experiments were conducted.

a) The substance was heated in a flask with a reflux condenser on the boiling water bath with an excess of 2% sulfuric acid for 6 hours. This gave a light yellow oil, which was washed with water free from traces of sulfuric acid. The oil was kept in vacuum and analyzed for nitrogen.

6.617 mg substance: 0.474 ml N_2 (20.5°, 731 mm).
Found %: N 8.00

$$\left.\begin{array}{l} C_6H_5(CH)_2(NO_2)_2CO_2C_2H_5. \\ C_6H_5(CH)_2NO_2(OH)CO_2C_2H_5. \\ C_6H_5(CH)_2(NO_2)_2CO_2H. \\ C_6H_5(CH)_2NO_2(OH)CO_2H. \end{array}\right\} \text{Computed \% N} \left\{\begin{array}{r} 10.45 \\ 5.86 \\ 11.67 \\ 6.64 \end{array}\right.$$

b) The addition product was heated on the boiling water bath for 6 hours with an 0.5 N alcoholic solution of caustic potash. After dilution with water, the solution was acidified with hydrochloric acid and extracted with ether. The solvent was removed to leave a yellow oil thicker and more viscous than water. Analysis gave the following results:

3.772 mg substance: 6.865 mg CO_2; 1.556 mg H_2O.
8.269 mg substance: 0.569 ml N_2 (21°, 731 mm).
Found %: C 49.66; H 4.62; N 7.69.

$$\left.\begin{array}{l} C_6H_5(CH)_2(NO_2)_2CO_2C_2H_5. \\ C_6H_5(CH)_2NO_2(OH)CO_2C_2H_5. \\ C_6H_5(CH)_2(NO_2)_2CO_2H. \\ C_6H_5(CH)_2NO_2(OH)CO_2H. \end{array}\right\} \text{Computed \%:} \left\{\begin{array}{l} C\ 49.25;\ H\ 4.47;\ N\ 10.45. \\ C\ 55.23;\ H\ 5.44;\ N\ 5.86. \\ C\ 45.0;\ \ H\ 3.33;\ N\ 11.67 \\ C\ 51.19;\ H\ 4.26;\ N\ 6.64. \end{array}\right.$$

More lengthy heating of the liquid addition product with an excess of alkali gave similar results.

The reduction of the liquid addition product of N_2O_4.

In a flask fitted with a reflux condenser, a thermometer, and a dropping funnel, there were placed 100.0 g of granulated tin and 20 ml of concentrated hydrochloric acid. The flask was cooled, and a small amount of a solution of the addition product in absolute alcohol was added (20.0 g of product in 50 ml of absolute alcohol). The addition of the product and of hydrochloric acid was continued in small portions. The temperature of the reaction mixture was not allowed to exceed 50°. When the calculated amount of hydrochloric acid and all the product had been added, the mixture was heated for 5 hours on the boiling water bath. The undissolved tin was removed. The liquid was diluted with 5 times the amount of water and the contents of the flask divided in two parts: the water-soluble and the water-insoluble.

Extraction with ether and driving off of the solvent gave 16.3 g of a thick, dark-colored ointment, which could not be made to crystallize. The ether-soluble portion had 10.68% of mineral residue.

5.172 mg substance: 10.90 mg CO_2; 2.19 mg H_2O.
4.312 mg substance: 0.052 ml N_2 (19°, 742 mm).
Found %: C 57.47; H 4.74; N 2.17.

Judging from the results of the analysis, the ether soluble portion was a complicated mixture, in all probability, of the original product, the tin salt of hydroxynitrocinnamic acid, of hydrocinnamic acid, and of other compounds whose nature could not be determined because of the impossibility of separating the mixture.

The water-soluble portion of the reduction product was treated with hydrogen sulfide until all the tin had precipitated. The filtrate from the tin sulfide was concentrated until the odor of hydrogen sulfide had disappeared. In order to decompose the remaining ethyl esters, the aqueous solution was heated for 8 hours on the water bath with barium hydroxide. When saponification was complete, the barium hydroxide was removed with sulfuric acid. The barium sulfate was filtered off and the filtrate evaporated to dryness. In order to remove ammonium chloride, the residue was treated in an extraction apparatus with absolute alcohol. The alcoholic solution was decolorized with animal charcoal, and the alcohol driven off in vacuum. The syrupy residue, on standing in the desiccator, formed colorless crystals, which were recrystallized from hot water with an m.p. of 302-306° (with decomposition). Yield 1.26 g. Analysis gave figures which corresponded to those for a mixture of hydroxyamino- and diaminocinnamic acids:

5.982 mg substance: 13.121 mg CO_2; 3.317 mg H_2O.
4.293 mg substance: 9.412 mg CO_2; 2.502 mg H_2O.
5.831 mg substance: 0.537 ml N_2 (19°, 737 mm).
5.342 mg substance: 0.498 ml N_2 (17°, 741 mm).
Found %: C 59.85, 59.80; H 6.21, 6.50; N 10.45, 10.70;

$$\left.\begin{array}{l} C_6H_5(CH)_2(NH_2)_2CO_2H. \\ C_6H_5(CH)_2(NH_2)_2(OH)CO_2H. \end{array}\right\}\text{Computed \%: }\begin{array}{lll} C\ 60.00; & H\ 6.67; & N\ 15.55 \\ C\ 59.67; & H\ 6.08; & N\ 7.73. \end{array}$$

The action of concentrated hydrochloric acid on a concentrated aqueous solution of these amino acids, followed by precipitation with a mixture of alcohol and ether, gave a white precipitate. The hydrochloride salt dissolved well in water, the aqueous solution showing an acid reaction. The crystals, after washing with alcohol and ether and standing in a desiccator over sulfuric acid, had m.p. 143-149.5°. A quantitative determination of halogen gave a value corresponding to that of a mixture of the hydrochlorides of diamino- and hydroxyaminocinnamic acids:

0.1261 g substance: 0.1192 g AgCl.
Found %: Cl 23.40.

$$\left.\begin{array}{l} C_9H_{14}O_2N_2Cl_2 \\ C_9H_{12}O_3NCl \end{array}\right\}\text{Computed \%: }\begin{array}{l} Cl\ 28.00 \\ Cl\ 16.32. \end{array}$$

Thus, on the basis of our investigation, we may assume that the action of gaseous nitrogen peroxide on the ethyl ester of cinnamic acid gives a mixture consisting of the addition products of NO_2-NO_2 and NO_2-ONO.

An investigation of the crystalline addition product of N_2O_4

This compound was in the form of beveled platelets with a blue color, soluble in 50% ethyl alcohol and in ethyl acetate (the acetate solution had a blue color). The product was slightly soluble in benzene, ether, and acetone; it was insoluble in chloroform, carbon tetrachloride, and ethyl, propyl, butyl, and amyl alcohols. Upon heating in a capillary, the product melted at 132-133° to give a faintly blue liquid, which on further heating (to 162°) decomposed with the evolution of a brown gas. Upon heating on a metal spatula, the substance burned with detonation.

4.312 mg substance: 7.820 mg CO_2; 1.950 mg H_2O.
4.232 mg substance: 7.650 mg CO_2; 1.866 mg H_2O.
6.328 mg substance: 0.608 ml N_2 (22°, 744 mm).
5.954 mg substance: 0.561 ml N_2 (20°, 741 mm).
Found %: C 49.45, 49.30; H 5.06, 4.93; N 10.90, 10.70.
$C_{11}H_{12}O_6N_2$. Computed %: C 49.25; H 4.47; N 10.45.

When the crystalline product was heated with a 0.5 N alcoholic solution of caustic potash on the water bath for 5 hours, the ester was saponified, and split off a single group containing nitrogen. Upon acidification with hydrochloric acid, extraction with ether, and removal of the solvent, a yellow oil was obtained. This was soluble in ether, alcohol, and ethyl acetate (the acetate solution had a pale blue color) and insoluble in petroleum ether. Analysis for nitrogen gave a result corresponding to that for nitrosohydroxycinnamic acid:

5.691 mg substance: 0.364 ml N_2 (18.5°, 740 mm).
Found %: N 7.29.
$C_9H_9O_4N$. Computed %: N 7.18.

The crystalline addition product was reduced with tin in hydrochloric acid. This gave, from 2.5 g of product, 0.5 g of a crystalline material which was soluble in water, better in hot water than in cold. The colorless crystals were recrystallized from water. Upon heating in an open capillary, they turned yellow at 287°, darkened at 300°, and did not melt at 326°. Upon heating on a metal spatula the substance burned completely. With concentrated hydrochloric acid it gave a hydrochloride, which melted at 167-170°.

5.635 mg substance: 0.382 ml N_2 (17.5°, 730 mm).
Found %: N 7.65.
$C_9H_{11}O_3N$. Computed %: N 7.73, corresponding to aminohydroxycinnamic acid.

We obtained α-aminohydroxycinnamic acid by reducing the product of the action of N_2O_4 on cinnamic acid. It had m.p. 315-317° (with decomposition) and its hydrochloride melted at 148-150°.

The aminohydroxycinnamic acid we had obtained by reducing the crystalline addition product formed by N_2O_4 and the ethyl ester of cinnamic acid had different properties, both with regard to its own behavior, and to its hydrochloride, which melted at 167-170°. This made it seem that the acid obtained might be β-amino-α-hydroxycinnamic acid. As for the crystalline addition product of N_2O_4, this, on the basis of the results obtained and of the totality of its properties, might be characterized as a secondary nitrosate of the ethyl ester of cinnamic acid.

II. The action of liquid nitrogen peroxide on ethyl cinnamate

To a solution of 15.0 g of ethyl cinnamate in 40 ml of absolute ether, nitrogen peroxide was added at 0° in small portions over a period of 5 hours. The first portion of N_2O_4 did not raise the temperature; obviously, the nitrogen peroxide dissolved in the ether. After the second portion of N_2O_4 had been added, the temperature of the solution rose to 7°. The temperature was again brought down to 0° by vigorous cooling. During subsequent additions of nitrogen peroxide, the temperature of the solution did not rise above 3°. As more and more nitrogen peroxide was added, the solution gradually turned from green to yellow; at the end of the reaction, the solution had turned dark brown. A total of 27.0 g of nitrogen peroxide was added, basing the calculation on the addition of N_2O_4 not only to the double bond of the side chain, but to the benzene nucleus. At the end of the reaction, the flask and its contents were kept for 3 hours in the cooling mixture, and then allowed to stand overnight in ice water. On the following day the solution was filtered. The filtrate was transferred to a porcelain dish, which was placed in a porcelain desiccator submerged in ice water. Here the solvent and the excess of N_2O_4 were removed by the passage of dry air. Removal of the solvent gave 22.4 g of a thick amber-yellow oil. The gain in weight (7.4 g) almost corresponded to the theoretical gain in weight calculated for the addition of one molecule of N_2O_4 to ethyl cinnamate. The iodine number of the product obtained was zero. Upon standing in the desiccator over sulfuric acid, by the third day the oil had formed a considerable quantity of light blue crystals, which could not be separated by ordinary filtration from the oily portion. The mixture was therefore treated with absolute alcohol. The liquid portion dissolved in this, and the crystals did not dissolve. Removal of the alcohol gave 7.9 g of a yellow oil. Investigation of the liquid substance indicated that it was identical with the liquid product of the action of gaseous nitrogen peroxide on ethyl cinnamate, i.e., that it was a mixture of the addition products NO_2-NO_2 and NO_2-ONO.

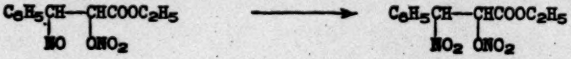
The crystalline product dissolved in ethyl acetate, but was not completely soluble in 50% alcohol. It dissolved slightly in benzene and acetone and was insoluble in chloroform, carbon tetrachloride, ethyl alcohol, and propyl, butyl, and amyl alcohols. The product had m.p. 121-133°.* And, in fact, treatment with 50% alcohol gave two crystalline substances: one was soluble in 50% alcohol and the other was insoluble. The substance soluble in 50% alcohol (1.20 g) was in the form of beveled platelets with a blue color, melting at 132-133° to give a blue liquid.

4.293 mg substance: 0.401 ml N_2 (19°, 742 mm).
Found %: N 10.66.
$C_{11}H_{12}O_6N_2$. Computed %: N 10.45.

The nitrogen content corresponded to that of the nitrosonitrate of ethyl cinnamate. The blue color of the product disappeared upon prolonged standing. Thus, after 7 months of standing in a desiccator over sulfuric acid, the substance had turned colorless, while at the same time its properties and crystal form also changed. The colorless prismatic crystals did not dissolve in 50% alcohol, but dissolved well in ethyl acetate, without coloring the solvent blue. After recrystallization from ethyl acetate, the substance had m.p. 151-152°. Upon heating on a metal spatula, the product burned with detonation. Analysis of the colorless crystalline product for nitrogen gave a figure corresponding to that for the nitronitrate of ethyl cinnamate.

6.518 mg substance: 0.560 ml N_2 (19°, 741 mm).
Found %: N 9.79.
$C_{11}H_{12}O_7N_2$. Computed %: N 9.86.

The formation of the nitronitrate ester is easily explained by the fact that the nitrosate which is first formed lends a blue color to the product of the reaction, and then, upon oxidation, turns into the colorless nitronitrate:



$$C_6H_5\underset{NO}{CH}-\underset{ONO_2}{CH}COOC_2H_5 \longrightarrow C_6H_5\underset{NO_2}{CH}-\underset{ONO_2}{CH}COOC_2H_5$$

A second crystalline substance (6.4 g) was obtained by treating the addition product with 50% alcohol. This was in the form of colorless prismatic crystals, soluble in ethyl acetate and insoluble in alcohol. This preparation was recrystallized from ethyl acetate with an m.p. of 151-152°. It had no blue color in the molten condition and upon solution did not color ethyl acetate blue.

5.698 mg substance: 0.498 ml N_2 (20°, 743 mm).
Found %: N 9.95.
$C_{11}H_{12}O_7N_2$. Computed %: N 9.86.

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*Judging from the melting point, this product was not a single compound.

Upon heating the crystalline compound on the water bath for 5 hours with an excess of a 0.5 N alcoholic solution of caustic potash, then acidifying with hydrochloric acid, and extracting with ether, an amber-yellow oil was obtained. This was soluble in alcohols, and in ethyl acetate, insoluble in petroleum ether. The oil was washed with petroleum ether and then used for a quantitative detemination of nitrogen.

4.731 mg substance: 0.277 ml N_2 (23°, 740 mm).
Found %: N 6.57.
$C_9H_9O_5N$. Computed %: N 6.64.

Thus, the crystalline addition product of nitrogen peroxide to ethyl cinnamate was saponified upon heating with alkali, and split off a single nitrogen-containing group. Upon reduction with tin and hydrochloric acid, 3.2 g of the crystalline product (with m.p. 151-152°) gave 0.65 g of a colorless crystalline substance. This was more soluble in hot water than in cold. Upon heating on a metal spatula, this substance burned completely. When heated in an open capillary, the compound turned yellow at 286°, darkened at 302°, but did not melt even at 325-327°.

5.068 mg substance: 0.343 ml N_2 (18.5°, 729 mm).
Found %: N 7.60.
$C_6H_5CHNH_2CHOHCO_2H$. Computed %: N 7.73.

The reduced product reacted with concentrated hydrochloric acid to give the hydrochloride, which was very soluble in water. The aqueous solution of the salt had an acid reaction to litmus. The hydrochloride, washed with ether and kept in a desiccator, had m.p. 168-170°.

0.1318 g substance: 0.0862 g AgCl.
Found %: Cl 16.19.
$C_9H_{12}O_3NCl$. Computed %: Cl 16.32.

Therefore, on the basis of the results of investigation, its properties as a whole, and a comparison with the previously obtained compounds, the crystalline addition product (m.p. 151-152°) may be characterized to be the nitronitrate of ethyl cinnamate. The formation of the nitronitrate of the ester makes it possible to conclude that along with the addition of the liquid nitrogen peroxide, oxidation also takes place.

SUMMARY

1. The ethylene bond of the side chain of the ethyl ester of cinnamic acid is completely saturated both by gaseous and by liquid nitrogen peroxide.

2. The action of gaseous nitrogen peroxide gave liquid and crystalline addition products. Both products were investigated.

3. The action of liquid nitrogen peroxide on the ethyl ester of cinnamic acid gave a liquid addition product and two crystalline compounds which differed in their properties and structure.

4. It has been shown that the action of gaseous and of liquid nitrogen peroxide on the ethyl ester of cinnamic acid gives a blue crystalline product in both cases. This is a nitrosonitrate.

5. The reduction of the addition products gives the corresponding amino acids.

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THE SYNTHESIS AND STUDY OF THIO ANALOGUES OF THEOBROMINE

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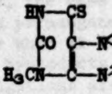
It has been shown by us previously that the action of phosphorus trisulfide on anhydrous caffein results in substituting either one or two atoms of oxygen in the latter by sulfur, with the formation of 6-thiocaffein and 2,6-dithiocaffeine [1].

The objective of the present work was to trace the influence of phosphorus polysulfides on another representative of the purine series, theobromine (3,7-dimethylxanthine). Here, by analogy, we might expect the formation of two mono-substituted products and of one dithio substituted, namely: 3,7-dimethyl-2-hydroxy-6-thiopurine (I), 3,7-dimethyl-2-thio-6-hydroxypurine (II), and 3,7-dimethyl-2,6-dithiopurine (III):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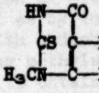
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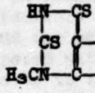
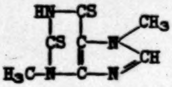

(III)

The first series of experiments, carried out with phosphorus trisulfide and theobromine in kerosene medium at a temperature of 190-210°, showed that in all cases, independent of the length of the experiment (from 1 hour to 2.5 hours) only 3,7-dimethyl-2,6-dithiopurine was obtained, i.e., that the substitution of both oxygen atoms by sulfur took place. When the temperature was lowered to 170-180°, the same product was formed. At 150-160°, the reaction between the substances indicated took place very slowly, and the product obtained consisted chiefly of unchanged theobromine, with some sulfur-containing material. In one case it was possible to determine the presence of 2.4% of sulfur in the reaction product, and in another 3.98%, whereas the monosubstituted theobromine required 16.33% and the dithio substituted compound, 30.19%. Therefore, phosphorus trisulfide replaces the oxygen by sulfur not stepwise but all or nothing, i.e., both atoms of oxygen are replaced at the same time. In caffeine, the oxygen in position 6 is distinguished by its greater mobility, and is substituted by sulfur in the first stage. This difference in the behavior of theobromine and caffeine may be explained by the presence in the first of a methyl group in position 1. E Fischer [2] had already noted that in the purine series the number of methyl groups has a great influence on the course of chemical reactions. We may also note that alcoholic alkali easily cleaves the pyrimidine ring of caffeine with the formation of thiocaffeidine, while many hours of boiling with alkali leave theobromine unchanged.

Various difficulties were encountered in the attempt to separate the thio products obtained in the reaction from unchanged theobromine. The general similarity of their chemical properties, and their virtual total insolubility in the usual organic solvents, made the usual methods of separation unsuitable. The product was obtained by means of the different solubilities in water of potassium theobrominate and potassium dithiotheobrominate. The first is very soluble in water at room temperature, while the second dissolves upon heating, and in considerable part crystallizes out after cooling.

The structure of the dithiotheobromine was shown not only by analysis, but also by methylation. This gave a product which in all its properties appeared identical with 2,6-dithiocaffeine. A mixed test of the methylated product with 2,6-dithiocaffeine obtained by the direct reaction of caffeine with phosphorus trisulfide gave no depression of the melting point.

During the methylation of the dithiotheobromine with dimethylsulfate, our attention was directed to the fact that in all the experiments, the amount of the desired dithiocaffeine was very small in comparison with the amount of starting materials used. We may note that a similar methylation of theobromine itself gives considerable yields of caffeine. This fact made us consider it probable that of the two desmotropic forms which dithiotheobromine may have, the lactam (IV) and the lactim (V), the latter must receive preference.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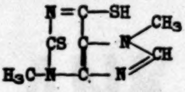
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A considerable number of other results also testify in favor of this conclusion. For instance, the ease of oxidation of dithiotheobromine in weakly alkaline medium by potassium permanganate as well as by iodine, the considerable evolution of hydrogen sulfide when it is heated with hydrochloric acid, and the mercaptan-like odor when the byproducts obtained by methylation are decomposed with acid. Our further investigations are intended to obtain a decisive answer to this question.

EXPERIMENTAL

3,7-Dimethyl-2 6-dithiopurine (III)

10 g of theobromine dried at 100°, mixed with 20 g of finely crushed phosphorus trisulfide and 150 ml of kerosene (fraction from 220-240°), was heated with energetic stirring in a flask fitted with a reflux condenser. The heating was continued for 1 hour at 180-200°. At the end of the reaction the contents of the flask were cooled to room temperature, the liquid removed by filtration, and the precipitate washed with ether (in order to remove the remaining kerosene).

The phosphorus polysulfide which had not reacted was decomposed by heating the precipitate with water.

The thioproduct obtained, mixed with a small amount of unreacted theobromine, was filtered, washed with hot water, and then treated with a 10% solution of caustic potash at 80-90°. After filtration and subsequent cooling, white plate-like crystals of potassium 2,6-dithiotheobrominate separated. These were filtered with suction, washed with a small quantity of water, and decomposed with dilute hydrochloric acid. The precipitate which formed was filtered off, washed with water and alcohol and dried at 100°. Yield 4-5 g, amounting to 34-42% of theory.

0.1247 g substance: 0.2670 g $BaSO_4$ (Messinger)
0.2843 g substance: 0.6220 g $BaSO_4$.
0.1318 g substance: 30.5 ml N_2 (12°, 753 mm).
0.1240 g substance: 27.7 ml N_2 (12°, 758 mm).
Found %: S 29.41, 30.05; N 27.1, 26.32.
$C_7H_8S_2N_4$. Computed %: S 30.19; N 26.41.
$C_7H_8OSN_4$. Computed %: S 16.32; N 28.57.

The 3,7-dimethyl-2,6-dithiopyrine was in the form of a light yellow powder with m.p. 290-292° (with decomposition), very slightly soluble in hot water, ether and chloroform. It dissolved upon heating in caustic alkalies, giving brown solutions.

Sodium dithiotheobrominate

3.2 g of dithiotheobromine was dissolved with heating in 10 ml of a 10% caustic soda solution. To the solution there was added 20 ml of alcohol. The precipitate which formed was washed with alcohol and ether and dried in a vacuum desiccator. 2.9 g of a sulfur-yellow powder was obtained (82% of theory). The aqueous solutions (2.5%) were slightly cloudy, and gradually hydrolyzed to form an insoluble precipitate.

0.3260 g substance: 0.0957 g Na_2SO_4.
0.3615 g substance: 0.1046 g Na_2SO_4.
Found %: Na 9.50, 9.34.
$C_7H_7N_4S_2Na$. Computed %: Na 9.83.

The methylation of 3,7-dimethyl-2,6-dithiopurine

2.1 g of dithiotheobromine was dissolved with heating in 5 ml of a 10% solution of caustic soda. After cooling, 3 ml of dimethylsulfate was added in small portions, with cooling and stirring. The excess of the latter was destroyed by the subsequent addition of a solution of caustic soda. The precipitate was extracted with chloroform and precipitated by the addition of alcohol. A second crystallization from chloroform gave 0.3 g of a substance which from its appearance and its other physical properties corresponded to the previously described dithiocaffeine [1]. Its melting point was 225-226°. A mixed test gave 224-226°.

SUMMARY

1. Conditions have been discovered for the preparation of 3,7-dimethyl-2,6-dithiopurine from theobromine by the action of phosphorus trisulfide. The compound's physico-chemical properties have been investigated and its structure shown.

2. Methylation of dithiotheobromine has given the previously described dithiocaffeine. The question of the most probable lactim structure of dithiotheobromine has been considered.

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THE SYNTHESIS OF ESTERS OF NAPHTHYLMETHYLPHOSPHINIC ACIDS

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In the development of our previous work on the synthesis of esters of phosphinic acids by the action of triethyl phosphite or sodium diethyl phosphite on chloromethyl derivatives of aromatic compounds [1], we obtained analogous forms of esters of phosphinic acids which contained the naphthalene nucleus.

The literature gives the synthesis of only 1-naphthylmethylphosphinic acid and its ethyl ether by the action of triethyl phosphite on 1-chloromethylnaphthalene [2].

The action of triethyl phosphite on 2-bromomethylnaphthalene gave us the isomeric ethyl ester of 2-naphthylmethylphosphinic acid (I) in the form of a viscous, colorless liquid with the following characteristics: b.p. 170-172° at 1 mm; n_D^{20} 1.5583; d_{20}^{20} 1.1483.

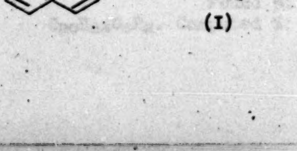
Saponification of the ester gave 2-naphthylmethylphosphinic acid with m.p. 229-230°. 2-Naphthylmethylphosphinic acid has a higher melting point than 1-naphthylmethylphosphinic acid (212-212.5°).

As has recently been shown [2], in the chloromethylation of naphthalene, when two chloromethyl radicals are introduced, the chief product of the reaction is 1,4-bis-chloromethylnaphthalene, along with a small quantity of 1,5-bis-chloromethylnaphthalene.

The action of triethyl phosphite on 1,4-bis-chloromethylnaphthalene gave us the ethyl ester of 1,4-diphosphonemethylnaphthalene (II) in the form of a viscous, undistillable liquid. Hydrolysis of the ester gave the free acid, with m.p. 276-279°.

The chloromethylation of tetralin led to the formation of 5,8-bis-chloromethyl-1,2,3,4-tetrahydronaphthalene [3].

The action of triethyl phosphite on this permitted us to synthesize the ethyl ester of 5,8-diphosphonemethyl-1,2,3,4-tetrahydronaphthalene (III). The ester was a viscous liquid: b.p. 254-255° at 6 mm and n_D^{20} 1.5146. Its hydrolysis gave the free acid with m.p. 296-300°.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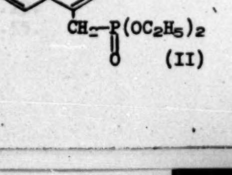
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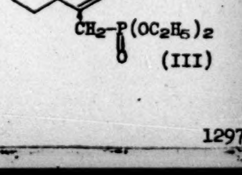
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EXPERIMENTAL

The action of 2-bromomethylnaphthalene on triethyl phosphite

In a small distilling flask there was placed 3 g of 2-bromomethylnaphthalene (m.p. 52-53°) [4]. The flask was heated on a metal bath until the temperature inside it was 140-150°. 2.9 g of triethyl phosphite was dropped into the bromo-compound over a period of 15 minutes. The temperature was raised to 170-180°. The heating was continued until there was no more evolution of ethyl bromide. The contents of the flask were distilled in vacuum to give a fraction containing the ethyl ester of 2-phosphonemethylnaphthalene (I) in the form of a viscous liquid. Yield 3.3 g, or 87.3% of theory:

B.p. 170-172° at 1 mm; n_D^{20} 1.5583; d_{20}^{20} 1.1483.

0.0956 g substance: 20.1 ml NaOH (titer 0.01848).
Found %: P 10.76.
$C_{15}H_{19}O_3P$. Computed %: P 11.15.

The hydrolysis of the ester. 0.9 g of the ester was heated with 8 ml of dilute hydrochloric acid (1:1) in a sealed tube at 125-135° for 5 hours. 0.7 g (98.6%) of 2-phosphonemethylnaphthalene was obtained in the form of crystals with m.p. 229-230°, (on block). Recrystallization from water by heating in a sealed tube at 140° gave colorless shining platelets.

0.0566 g substance: 15.35 ml NaOH (titer 0.01848).
Found %: P 13.88.
$C_{11}H_{11}O_3P$. Computed %: P 13.96.

The action of 1,4-bis-chloromethylnaphthalene on triethyl phosphite

To 1.7 g of bischloromethylnaphthalene (m.p. 143-145°) [3], heated in a small flask to 150-155°, there was added 3.5 g of triethyl phosphite over a period of 15 minutes. In order to complete the reaction, the flask was heated for 1 hour at 200-205°. After the unreacted triethyl phosphite had been distilled off in vacuum, there remained in the flask 3.2 g of the ethyl ester of 1,4-diphosphonemethylnaphthalene in the form of a very viscous liquid, which could not be distilled at a pressure of 3 mm.

The ester (1.3 g) was heated with 14 ml of dilute hydrochloric acid (1:1) in a sealed tube at 130-135° for 8 hours. 0.9 g (93.7%) of 1,4-diphosphonemethylnaphthalene was obtained with m.p. 275-278° (block). Recrystallization from water by heating in a sealed tube to 135° gave colorless scales with m.p. 276-279° after preliminary softening (block).

0.0636 g substance: 24.32 ml NaOH (titer 0.01848).
Found %: P 19.57.
$C_{12}H_{14}O_6P_2$. Computed %: P 19.61.

The action of triethyl phosphite on 5,8-bis-chloromethyl-1,2,3,4-tetrahydronaphthalene

To 2.4 g of bischloromethyltetralin (m.p. 117°)[3] heated to 145-155°, there was added over a period of 15 minutes 4.2 g of triethyl phosphite. The heating was continued for 1 hour at this temperature and 1 hour at 200-210°. The residue in the flask was distilled in vacuum and gave a fraction containing the ester of 5,8-diphosphonemethyl-1,2,3,4-tetrahydronaphthalene in the form of 3.0 g of a viscous liquid, soluble in water (66.3%). B.p. 254-255° at 6 mm; n_D^{20} 1.5146.

0.1158 g substance: 32.1 ml NaOH (Titer 0.01848).
Found %: P 14.19.
$C_{20}H_{34}O_6P_2$. Computed %: P 14.35.

Hydrolysis of the ester. 1.3 g of the ester was heated with 13 ml of dilute hydrochloric acid (1:1) in a sealed tube for 8 hours at 130-135°. 0.9 g of 5,8-diphosphonemethyl-1,2,3,4-tetrahydronaphthalene (93.7%) was obtained. Recrystallization by heating with water in a sealed tube to 135° gave fine colorless little needles with m.p. 296-300° after preliminary softening (block).

0.0630 g substance: 24.95 ml NaOH (titer 0.01848).
Found %: P 20.27.
$C_{12}H_{18}O_6P_2$. Computed %: P 19.37.

SUMMARY

By the action of triethyl phosphite on 2-bromomethylnaphthalene, 1,4-bischloromethylnaphthalene, and 5,8-bischloromethyl-1,2,3,4-tetrahydronaphthalene, the esters of 2-phosphonemethylnaphthalene, 1,4-diphosphonemethylnaphthalene, and 5,8-diphosphonemethyl-1,2,3,4-tetrahydronaphthalene have been synthesized.

The hydrolysis of these esters gave the corresponding acids.

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ON OXIDATION BY MANGANESE TRIACETATE

II. A STUDY OF THE OXIDATION OF α-GLYCOLS AND α KETOALCOHOLS

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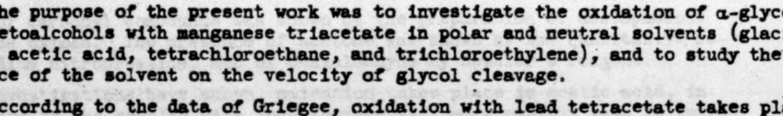
R. Griegee and his coworkers [1], in their investigation of the oxidation of α-glycols in various solvents, came to the conclusion that lead tetracetate was a uniformly thorough oxidizing agent for the production of glycol cleavage. The acetates of other metals, like manganese, cobalt, and thallium, were, in their opinion unsuitable in practice because of the considerably lower oxidizing potential. However, the authors gave no experimental data on oxidation with manganese, cobalt, and other acetates.

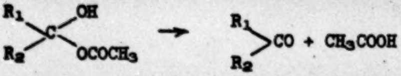
The purpose of the present work was to investigate the oxidation of α-glycols and α-ketoalcohols with manganese triacetate in polar and neutral solvents (glacial and 80% acetic acid, tetrachloroethane, and trichloroethylene), and to study the influence of the solvent on the velocity of glycol cleavage.

According to the data of Griegee, oxidation with lead tetracetate takes place more rapidly in neutral solvents. For example, glycol cleavage took place in acetic acid at a fraction of a thousandth of the velocity of cleavage in tetrachlorpethane or in benzene. Griegee explained the comparative inertness of acetic acid by the mechanism of the oxidation. The reaction took place with the formation of intermediate products of a cyclic structure – lead glycolates, which were stable in acetic acid.

This mechanism of oxidatinn was out of the question for manganese triacetate, as even if an intermediate of a cyclic character were formed, cleavage of the latter would give a manganese monoacetate.

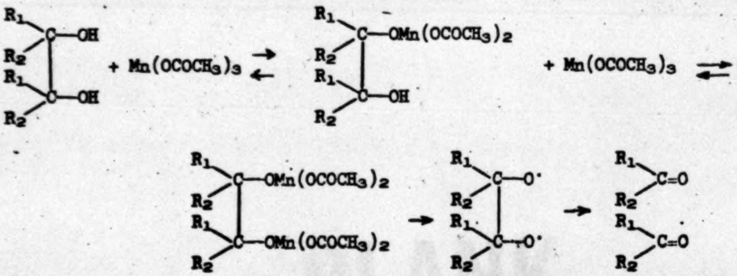
In one of our articles [2] we expressed the hypothesis that in oxidation with manganese triacetate, the incomplete acetate of the hydrated form of the ketone might be formed as an intermediate product. In a subsequent phase, this would be decomposed to give the carbonyl compound and acetic acid, according to the mechanism (I):





However, this reaction mechanism does not explain the inertness of the acetates of benzopinacone and hydrobenzoin to manganese triacetate. As our experiments have shown, these acetates are not oxidized even at a temperature of 100° (the activity of the solution was unchanged after 9 hours of heating).

The partial acetates were oxidized at 100° only to the extent of 15%. In view of the experimental results, it is more plausible to assume that the reaction proceeds according to the following mechanism (II):



The formation of carbonyl compounds was shown by the preparation of acetophenone and benzophenone oximes. The presence of acetone was shown by the qualitative reaction with sodium nitroprusside, and of benzaldehyde by Nessler's reagent.

As our investigations have shown, oxidation takes place in acetic acid, in contradistinction to the results with lead tetracetate, more rapidly than in tetrachloroethane. The velocity of oxidation is influenced, not only by the solvent and temperature, but by the structure of the compound to be oxidized. For example, the substitution of methyl radicals by phenyl increases the velocity of glycol cleavage.

Judging from the velocity of oxidation in glacial acetic acid, tertiary glycols must decompose in the following order: tetraphenylethylene glycol, symm. dimethyldiphenylethylene glycol, trimethylphenylethylene glycol, tetramethylethylene glycol, α-dihydroxydicyclopentyl and α-hydroxycyclohexyl carbinol.

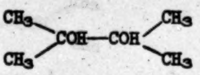
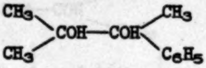
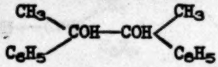
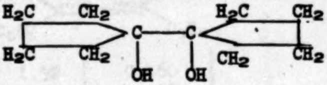
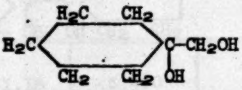
At a temperature of 30°, tetraphenylethylene glycol was oxidized to the extent of 84%, symm. dimethyldiphenylethylene glycol to 81%, trimethylphenylethylene glycol 68%, tetramethylethylene glycol 25%, and α-dihydroxydicyclopentyl 30%. At 30°, α-hydroxycyclohexylcarbinol was not oxidized (cf. Table 1).

In 80% acetic acid (in more dilute acid, heating caused the hydrolysis of the manganese triacetate), as in glacial, the same regularities of oxidation were observed, but the reactions took place much more slowly. For example, at a temperature of 30°, only tetraphenyl- and symm. dimethyldiphenylethylene glycols were partially oxidized. Trimethylphenylethylene glycol was oxidized only at 50°, and tetramethylethylene glycol at 80°. α-Dihydroxydicyclopentyl was 78% oxidized at 80°, and α-hydroxycyclohexylcarbinol 31.0%. In this case, apparently, the velocity of oxidation is influenced by the position of the hydroxyl groups.

In 80% acetic acid, the ditertiary glycols (benzopinacone) were oxidized more rapidly than the disecondary (hydrobenzoin). At 30°, hydrobenzoin was 29% oxidized, benzopinacone 57%, (cf. Table 2).

TABLE 1

The oxidation of α-glycols in glacial acetic acid

Temp., °	Time, hrs.	Amount $Na_2S_2O_3$, ml	$Mn(OCOCH_3)_2$ %	% of glycol oxidized	Temp., °	Time, hrs.	Amount $Na_2S_2O_3$, ml	$Mn(OCOCH_3)_2$	% of glycol oxidized
									
30	–	1.08	0.460		30	–	1.17	0.460	
	0.5	0.85	0.362			–	0.80	0.314	
	1.5	0.82	0.345	25		0.5	0.59	0.237	
50		0.74	0.315			1.5	0.48	0.188	
	2.0	0.50	0.213			2.0	0.39	0.153	68
	3.0	0.35	0.149		50	2.5	0.26	0.102	
	3.5	0.32	0.136	78		3.5	0.18	0.071	
						5.0	0.05	0.020	95
									
30	–	1.15	0.460		30	–	1.17	0.460	
	–	0.73	0.292			0.5	0.95	0.373	
	0.25	0.35	0.140			1.5	0.82	0.322	30
	0.50	0.24	0.096		50	–	0.79	0.310	
	1.00	0.22	0.088	81		2.0	0.60	0.236	
50	–	0.12	0.048			3.0	0.47	0.185	
	1.5	0.08	0.032			3.5	0.48	0.185	60
	2.0	0.06	0.021	95					
									
					30	–	1.06	0.460	
						0.5	1.06	0.460	
					50	–	1.05	0.460	
						1.0	0.91	0.395	
						1.5	0.85	0.369	20

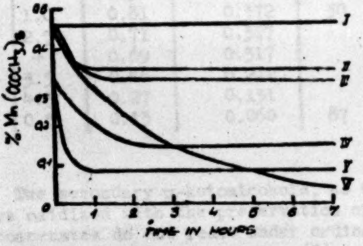
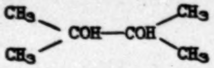
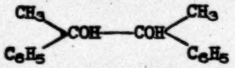
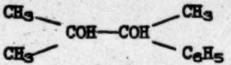
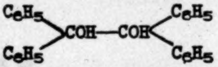
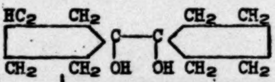


Fig. 1, Oxidation in glacial acetic acid at a temperature of 30°.

I-Hydroxycyclohexylcarbinol; II-pinacone; III-dihydroxydicyclopentyl; IV-trimethylphenylethylene glycol; V-dimethyldiphenylethylene glycol; VI-benzopinacone.

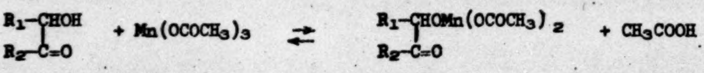
TABLE 2

The velocity of oxidation of α-glycols in 80% acetic acid

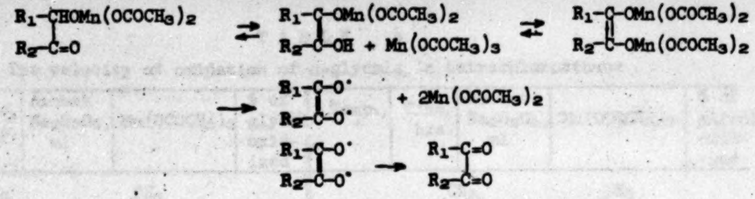
Temp. °	Time, Hrs	Amount $Na_2S_2O_3$, ml	$Mn(OCOCH_3)_3$	% of glycol ozidized
				
80	–	1.09	0.460	
	0.5	0.82	0.346	
	1.0	0.49	0.207	
	2.0	0.19	0.080	
	2.5	0.19	0.080	82
100	–	0.14	0.059	
	3.0	0.11	0.046	
	3.5	0.06	0.026	95
				
30	–	1.16	0.460	
	0.25	0.92	0.365	
	0.75	0.73	0.290	
	1.25	0.67	0.266	42
50	–	0.56	0.222	
	1.50	0.39	0.155	
	2.0	0.14	0.055	
	2.5	0.06	0.024	95
C_6H_5-CHOH-CHOH-C_6H_5				
30	–	0.98	0.460	
	1.0	0.81	0.372	30
	2.5	0.71	0.327	
50	–	0.69	0.317	
	3.5	0.46	0.212	
	4.5	0.27	0.131	
	0.5	0.13	0.060	87
				
50	–	1.14	0.460	
	0.5	0.88	0.411	
	1.5	0.70	0.284	
	2.0	0.61	0.245	47
80	–	0.46	0.185	
	2.5	0.28	0.113	
	3.0	0.12	0.048	
	3.5	0.04	0.016	96
				
30	–	1.32	0.460	
	–	0.77	0.268	
	0.5	0.76	0.265	57
50	1.0	0.75	0.263	
80	–	0.74	0.260	
	2.0	0.47	0.164	
	3.0	0.11	0.038	
	3.5	0.07	0.024	95
				
80	–	1.16	0.460	
	–	1.05	0.417	
	0.5	0.91	0.361	
	2.0	0.67	0.260	
	1.0	0.40	0.159	
	3.0	0.26	0.103	78

The secondary α-ketoalcohols, as distinguished from the α-glycols, were always oxidized with the preservation of the carbon skeleton, giving α-diketones. α-Ketoacetates do not react under ordinary conditions with manganese triacetate. Therefore, mechanism of reaction (I) is not applicable to α-ketoalcohols.

In our opinion, the oxidation of α-ketoalcohols takes place according to the following scheme:



$$\begin{matrix} R_1-CHOH \\ | \\ R_2-C{=}O \end{matrix} + Mn(OCOCH_3)_3 \rightleftarrows \begin{matrix} R_1-CHOMn(OCOCH_3)_2 \\ | \\ R_2-C{=}O \end{matrix} + CH_3COOH$$



$$\begin{array}{l}R_1-CHOMn(OCOCH_3)_2\\ \quad\;\, |\\ R_2-C{=}O\end{array} \rightleftarrows \begin{array}{l}R_1-C-OMn(OCOCH_3)_2\\ \quad\;\, \|\\ R_2-C-OH\end{array} + Mn(OCOCH_3)_3 \rightleftarrows \begin{array}{l}R_1-C-OMn(OCOCH_3)_2\\ \quad\;\, \|\\ R_2-C-OMn(OCOCH_3)_2\end{array}$$

$$\longrightarrow \begin{array}{l}R_1-C-O^{\cdot}\\ \quad\;\, |\\ R_2-C-O^{\cdot}\end{array} + 2Mn(OCOCH_3)_2$$

$$\begin{array}{l}R_1-C-O^{\cdot}\\ \quad\;\, |\\ R_2-C-O^{\cdot}\end{array} \longrightarrow \begin{array}{l}R_1-C{=}O\\ \quad\;\, |\\ R_2-C{=}O\end{array}$$

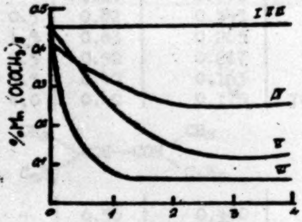


Fig. 2. Oxidation in 80% acetic acid at a temperature of 50°.

I-Pinacone; II-dihydroxydicyclopentyl; III-hydroxycyclohexylcarbinol; IV-trimethylphenylethylene glycol; V-hydrobenzoin; VI-dimethylphenylethylene glycol.

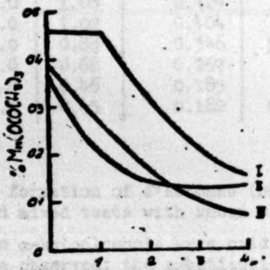


Fig. 3. Oxidation in 80% acetic acid at a temperature of 80°.

I-Anisoin; II-furoin; III-benzoin.

TABLE 3

The velocity of oxidation of α-ketoalcohols in 80% acetic acid

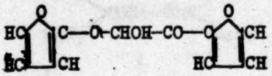
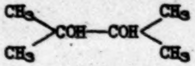
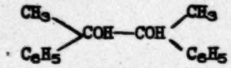
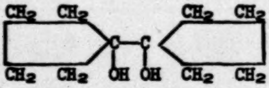
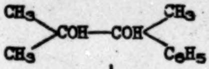
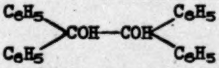
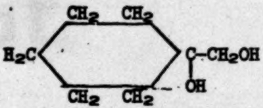
Temp., °	Time, Hrs.	Amount $Na_2S_2O_3$, ml	$Mn(OCOCH_3)_3$	% of glycol oxidized
				
30	-	1.06	0.460	
	0.5	1.02	0.443	
50	-	0.97	0.414	
	1.0	0.98	0.418.	12
80	-	0.96	0.410	
	1.5	0.72	0.316	
	2.0	0.64	0.278	
	3.0	0.39	0.170	
	4.0	0.31	0.133	72
$C_6H_5—CHOH—CO—C_6H_5$				
50	-	1.10	0.460	
	0.5	0.93	0.388	5
80	-	0.90	0.376	
	1.0	0.77	0.322	
	2.0	0.58	0.242	
	3.0	0.31	0.129	
	4.0	0.21	0.088	
	5.0	0.16	0.064	90
$CH_3O—C_6H_4—CHOH—CO—C_6H_4OCH_3$				
80	-	1.04	0.460	
	1.0	1.03	0.455	
	2.0	0.72	0.318	
	3.0	0.47	0.207	
	4.0	0.34	0.150	
	5.0	0.23	0.102	
	6.0	0.12	0.053	89

TABLE 4

The velocity of oxidation of α-glycols in tetrachloroethane

Temp., °	Time, hrs.	Amount $Na_2S_2O_3$, ml	$Mn(OCOCH_3)_3$	% of glycol oxidized
				
80	-	1.10	0.460	
	0.5	0.82	0.343	
	1.5	0.63	0.263	
	2.5	0.52	0.217	
	3.5	0.40	0.163	
	4.0	0.42	0.175	70
				
80	-	0.36	0.460	
	0.5	0.26	0.332	
	1.5	0.22	0.281	39
100	-	0.20	0.256	
	2.75	0.13	0.166	
	3.75	0.13	0.166	
				
80	-	1.17	0.460	
	1.0	1.08	0.424	
	2.0	1.02	0.404	
	3.0	0.88	0.346	34
100	4.0	0.68	0.267	
	5.0	0.46	0.185	
	6.0	0.45	0.182	61

Temp., °	Time, hrs.	Amount $Na_2S_2O_3$, ml	$Mn(OCOCH_3)_3$	% of glycol oxidized
				
80	-	1.09	0.444	
	1.0	0.98	0.399	
	2.0	0.78	0.317	
	3.0	0.63	0.256	
	4.0	0.65	0.257	47
				
80	-	0.82	0.460	
	-	0.71	0.400	
	0.25	0.68	0.380	
	1.0	0.64	0.358	22
100	1.5	0.50	0.280	
	2.5	0.40	0.324	
	4.0	0.40	0.324	50
				
80	-	1.21	0.460	
	1.0	1.21	0.460	
	3.0	1.37	0.460	
	4.0	1.97	0.320	
	5.0	0.75	0.247	
	6.0	0.60	0.190	
	8.0	0.60	0.198	50

The formation of diketones (benzil and anisil) was shown by the melting points and mixed tests with known preparations of the diketones.

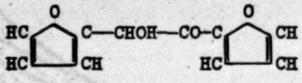
When α-ketoalcohols were oxidized in 80% acetic acid, the following regularities were observed: the substitution of an aromatic radical by a heterocyclic radical enabled the reaction to begin at a lower temperature; of the three keto-alcohols studied, only furoin was oxidized at 50°, to the extent of 12%, benzoin 5%, while anisoin was not oxidized at 50° (cf Table 3).

Fig. 3 shows the curves characterizing the oxidation velocity of the keto-alcohols at 80°.

Upon substituting the polar solvent by a neutral one (tetrachloroethane) the

TABLE 5

The velocity of oxidation of α-ketoalcohols in tetrachloroethane

Temp., °	Time, hrs.	Amount $Na_2S_2O_3$, ml	$Mn(OCOCH_3)_3$	% of glycol oxidized
				
80	-	1.20	0.460	
	-	0.94	0.360	
	1.0	0.60	0.250	
	2.0	0.47	0.180	
	3.0	0.37	0.142	76
100	-	0.37	0.142	
	4.0	0.22	0.084	
	5.0	0.18	0.069	
	6.0	0.20	0.076	83
C_6H_5—CHOH—CO—C_6H_5				
80	-	1.12	0.460	
	-	1.02	0.419	
	1.0	0.83	0.341	
	2.0	0.75	0.308	
	3.0	0.46	0.189	59.0
100	-	0.45	0.180	
	4	0.33	0.126	
	5	0.25	0.105	77.0
$CH_3OC_6H_4CHOH$—CO—$C_6H_4OCH_3$				
80	-	1.15	0.460	
	0.15	1.00	0.400	
	1.0	0.86	0.344	
	2.0	0.63	0.251	
	3.0	0.54	0.216	55
100	-	0.53	0.212	
	4.0	0.39	0.156	66

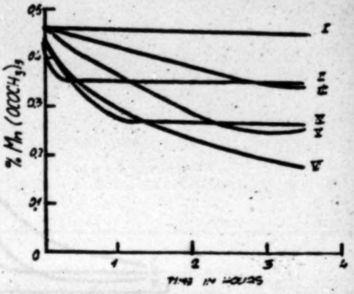


Fig. 4. Oxidation in tetrachloroethane at a temperature of 80°.
I-Hydroxycyclohexylcarbinol II-benzopinacone III-dihydroxycyclopentyl IV-dimethylphenylethylene glycol. V-trimethylphenylethylene glycol; VI-pinacone.

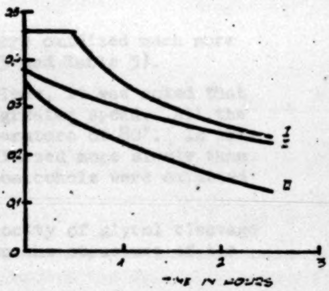


Fig. 5. Oxidation in tetrachloroethane at a temperature of 80°.
I-Anisoin II-benzoin; III-furoin.

velocity of oxidation is retarded, in contradistinction to what was found for lead tetracetate. In tetrachloroethane, in addition to the retardation of oxidation, the following regularities were observed: benzopinacone was oxidized more slowly than pinacone, while in acetic acid the aromatic radicals speeded up the oxidation; at a temperature of 80°, benzopinacone was 22% oxidized, while pinacone under the same conditions was 70% oxidized; at 80°, α-dihydroxydicyclopentyl was 34% oxidized, while α-hydroxycyclohexylcarbinol, at the same temperature, was unchanged (cf. Table 4).

Fig. 4 shows the curves which characterize the velocity of oxidation of α-glycols in tetrachloroethane.

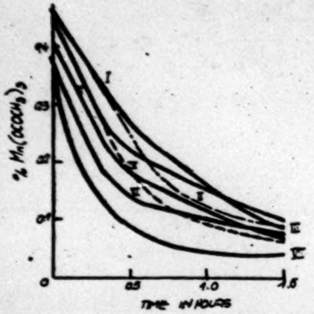


Fig. 6. Oxidation in trichloroethylene at a temperature of 80°.
I-Trimethylphenylethylene glycol. II-hydroxycyclohexylcarbinol III-pinacone IV-dihydroxydicyclopentyl V-benzopinacone VI-dimethyldiphenylethylene glycol. Vii-hydrobenzoin.

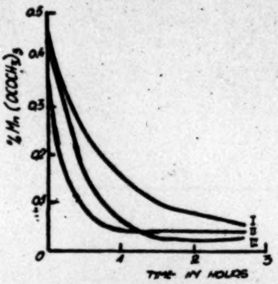


Fig. 7. Oxidation in trichlorcethylene at a temperature of 80°.

I-Anisoin; II-foroin; III-benzoin.

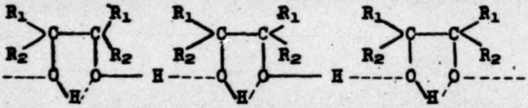
The α-ketoalcohols furoin, benzoin, and anisoin were oxidized much more slowly in tetrachloroethane than in acetic acid (cf. Fig. 5 and Table 5).

Upon replacing tetrachloroethane by trichloroethylene, it was noted that the oxidation of glycols and ketoalcohols took place with greater speed. All the glycols under investigation were 80-90% oxidized at a temperature of 80°. In trichloroethylene, as in glacial acetic acid, pinacone was oxidized more slowly than benzopinacone (cf. Fig. 6). In trichloroethylene, the ketoalcohols were oxidized at about the same speed (cf. Fig. 7).

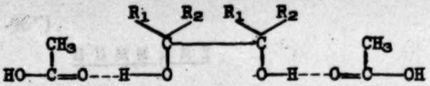
From these investigations it follows that the velocity of glycol cleavage in the presence of manganese triacetate depends not only on the structure of the glycol, but on the character of the solvent as well.

In polar solvents (glacial and 80% acetic acid) oxidation takes place under gentler conditions than in inert solvents.

This phenomenon, it seems to us, can be explained in the following manner: It is known that glycols, as well as alcohols, are associated under ordinary conditions by means of hydrogen bonds. The association of molecules may be pictured structurally in the following way:



In inert solvents, glycols are associated. In polar solvents, on the other hand, glycols are not associated, that is, they are in the form of monomers, as the glycol is attached to the acid by a hydrogen bond.



The interaction of the glycol with the solvent prevents the molecules from forming hydrogen bonds with each other, and therefore the glycols more easily undergo oxidation in a solution of acetic acid.

Attempts to study the velocity of the reaction in other solvents (dichloroethane, chloroform, carbon tetrachloride, acetone, methylethylketone, benzene, toluene, etc.) did not give positive results because of the low solubility of manganese triacetate in these solvents.

EXPERIMENTAL

All the experiments on oxidation were conducted in a three-necked flask, fitted with a mechanical stirrer and a reflux condenser, in a stream of carbon dioxide. The calculated amount of manganese acetate was first placed in the flask, and then 40-50 ml of solvent was added. The solution of the manganese triacetate took place during heating and stirring. The manganese triacetate dissolved comparatively well in glacial acetic acid. In order to dissolve the manganese triacetate in 80% acetic acid, it was necessary to work with especially great care, as hydrolysis took place upon prolonged heating at a temperature above 100°. After the manganese triacetate was dissolved, the activity of the solution was determined, and the glycol was then added.

In all the experiments, the glycol or ketoalcohol was used in amounts of 1/2000th to 1/4000th of a mole, and the manganese triacetate from 1/1000th to 1/2000th of a mole. Several experiments were carried out with each glycol (5 to 10).

Manganese triacetate dissolved only slightly in tetrachloroethane even upon heating. Solution was especially difficult in trichloroethylene.

For all the glycols investigated, the isolation of the products of oxidation was carried out in the following manner. At the end of the reaction, part of the acetic acid was driven off, and water added to the residue. The solution was then filtered. The filtrate was neutralized with a concentrated solution of soda or a 10% solution of alkali until the reaction was weakly alkaline. The solution was extracted with ether. The ether extract was dried over calcined sodium sulfate, and the ether then driven off. The residue was treated in the usual way with hydroxylamine hydrochloride.

Thus we obtained the oxime of benzophenone, with m.p. 134-136°, and the oxime of acetophenone, with m.p. 57-58°.

The oxidation of pinacone and trimethylphenylethylene glycol gave acetone, which was determined qualitatively in the acetic acid distillate with sodium nitroprusside.

Hydrobenzoin was oxidized to give benzaldehyde, which was detected qualitatively with Nessler's reagent.

The isolation of the oxidation products of the α-ketoalcohols was carried out in similar fashion after the ether had been driven off and the solid residue recrystallized from alcohol. We thus obtained benzil, with m.p. 93-94° (a mixed test melted at 92-94°); upon boiling with sodium alcoholate, benzil first gave a purple color, and was then decolorized, as a result of the formation of benzilic acid.

The oxidation of anisoin and similar treatment gave anisil, with m.p. 94-95°

(a mixed test gave m.p. 94-96°).

SUMMARY

1. The mechanism of oxidation of glycols by lead tetracetate suggested by Griegee and his coworkers is not applicable to manganese acetate. We have suggested a mechanism of oxidation of α-glycols and secondary α-ketoalcohols by manganese triacetate.

2. The velocity of oxidation is influenced by the structure of the compound to be oxidized, by the solvent, and by the temperature.

3. It has been shown that in polar solvents (glacial and 80% acetic acid) the velocities of oxidation of dihydric alcohols are arranged in the following order: benzopinacone, symm. dimethyldiphenylethylene glycol, trimethylphenylethylene glycol, tetramethylethylene glycol, α-dihydroxycyclopentyl, and α-hydroxycyclohexylcarbinol.

4. The velocity of oxidation is influenced by the concentration of the solvent; it has been shown that in 80% acetic acid, all the glycols and ketoalcohols investigated are oxidized more slowly than in glacial acetic acid.

5. Under the same conditions, ditertiary glycols are oxidized more rapidly than disecondary.

6. The character of the solvent influences the oxidizing potential of manganese triacetate. In particular, in the neutral solvents tetrachloroethane and trichloroethylene, glycols are oxidized more slowly than in acetic acid.

LITERATURE CITED

[1] R.Griegee, Ann., 507, 159 (1933).

[2] S.Zonis, Trans. Leningrad Institute of Technolcgy, No. 15, (1947)

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ON OXIDATION BY MANGANESE TRIACETATE

IV. THE ACTION OF MANGANESE TRIACETATE ON γ ACETYLENE GLYCOLS

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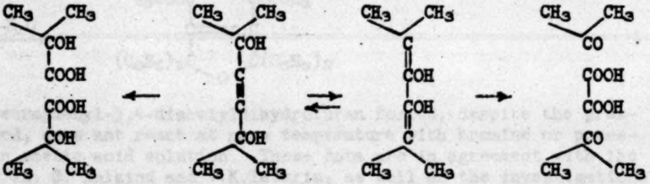
In previous papers [1] we have investigated the oxidation of carbinol and carbonyl derivatives by manganese triacetate. It has been found that secondary alcohols are oxidized only to the ketone stage, and that α-disecondary and ditertiary glycols are oxidized only with breaking of the carbon skeleton. Secondary α-ketoalcohols, even when an excess of oxidizing agent is used, form α-diketones.

The objective of the present work was to study the oxidation of γ-acetylene glycols with manganese triacetate. It was difficult to predict the mechanism of the reaction beforehand, as up to the time of our investigations manganese triacetate had not been used as an oxidizing agent for organic compounds.

It is known from the literature that the mechanism of the oxidation of γ-ditertiary acetylene glycols depends on the character of the oxidizing agent and on the reaction medium.

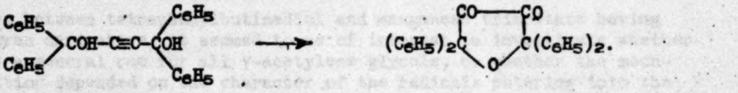
G. Dupont [2] found that the oxidation of acetylene glycols with potassium permanganate gave a mixture of products (hydroxyacids, ketones, oxalic acid).

According to Dupont, γ-acetylene glycols exist in two tautomeric forms:



V.N. Krestinsky [3] oxidized γ-acetylene glycols with potassium permanganate and likewise obtained oxalic acid.

P.A. Tikhomolov and coworkers [4] investigated the oxidation of tetraphenylbutinediol with chromic anhydride in glacial acetic acid, and obtained a cyclic diketone:



Yu. S. Zalkind and coworkers [5] obtained a similar compound by the oxidation of tetraphenylbutinediol with chromic anhydride. According to their results 2,2,5,5-tetraphenyl-3,4-dioxotetrahydrofuran was very difficult to crystallize and formed raspberry-colored crystals with m.p. 109-110°.

T.I.Temnikova and coworkers [6] investigated the oxidation of tetratolylbutinediol by chromic anhydride in 95% acetic acid; these authors obtained a cyclic diketone, also of a raspberry color.

K.Bowden and coworkers [7] obtained a mono and a diketone of the acetylene series by the oxidation of secondary alcohols or disecondary glycols with chromic anhydride in acetone solution. As these authors showed, the character of the solvent, the concentration, and the temperature influence the yield of ketones.

We may assume that in our case, γ-ditertiary acetylene glycols will be oxidized by manganese triacetate according to one of the above schemes.

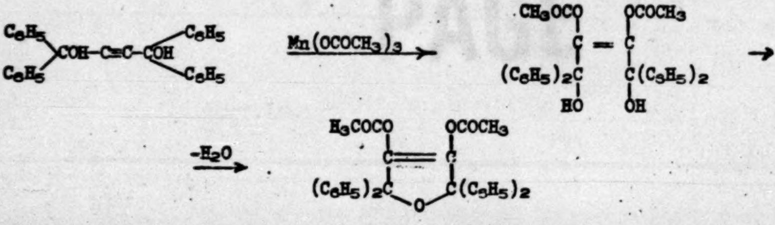
However, as our investigations have shown, only γ-disecondary acetylene glycols (diphenylbutinediol) are oxidized by manganese triacetate in glacial acetic acid to give γ-diketones (diphenylbutinedione).

γ-Ditertiary glycols – tetraphenylbutinediol – under these conditions are oxidized to give a yellow product with m.p. 189-190°; this does not react with hydroxylamine, phenylhydrazine, p-nitrophenylhydrazine, and o-phenylenediamine.

The Tserevitinov-Chugaev reaction gives a negative result. Acetic acid solutions of bromine and potassium permanganate are not decolorized, nor can a triple bond be detected.

Upon saponification and titration with an alcoholic solution of caustic potash, it was possible to show quantitatively that two acetyl groups were present.

On the basis of these results, we can suggest the following mechanism for the oxidation:



The 2,2,5,5-tetraphenyl-3,4-diacetyldihydrofuran formed, despite the presence of a double bond, does not react at room temperature with bromine or potassium permanganate in acetic acid solution. These data are in agreement with the results obtained by Yu. S. Zalkind and V.K.Teterin, as well as the investigations of E.D.Venus-Danilova.

In addition to 2,2,5,5-tetraphenyl-3,4-diacetyldihydrofuran, small amounts of benzophenone and tetraphenylbutinediol diacetate were obtained.

At the same time that we studied the oxidation, we also studied the reaction velocity.

The reaction between tetraphenylbutinediol and manganese triacetate having given a dihydrofuran derivative, it seemed to us of interest to investigate whether this reaction was a general one for all γ-acetylene glycols, or whether the mechanism of the reaction depended on the character of the radicals entering into the composition of the glycol.

As out experiments showed, manganese triacetate acts as an acetylating agent on the triple bond only in the case of γ-acetylene glycols of the aromatic or alkylaromatic series (tetraphenyl-, p-tetratolyl-, symm. diphenyl-p-ditolyl and symm. dimethyldiphenyl butinediol).

γ-Acetylene glycols of the aliphatic series – tetramethylbutinediol – are oxidized with much greater difficulty, and only with a rupture of the carbon skeleton, forming acetone and α-hydroxyisobutyric acid.

The different behaviors of γ-acetylene glycols which react with manganese triacetate can probably be explained by the conditions determining the temperature at which the reaction begins. For example, at 50°, of all the glycols investigated, only p-tetratolylbutinediol (66%) and symm. diphenylditolylbutinediol (74% and 32.5% depending on which stereoisomer is used) are oxidized. At 80°, tetraphenylbutinediol is 87% oxidized and dimethyldiphenylbutinediol 47% and 78% oxidized, depending on the stereoisomer used. Tetramethylbutinediol is oxidized only at 100°.

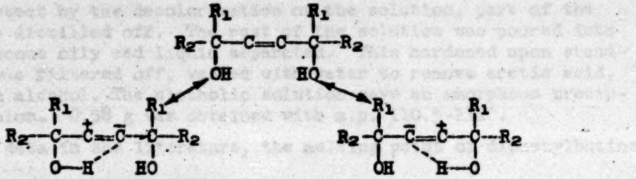
With regard to speed of oxidation, the glycols investigated can be arranged in the following order:

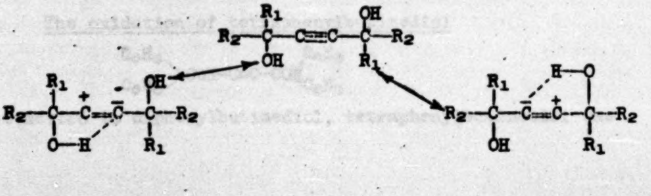
p-tetratolyl-, symm. diphenyl-p-ditolyl-, tetraphenyl-, symm. dimethyldiphenyl-, and tetramethyl- butinediol.

In addition to the nature of the radicals, the stereoisomerism of the glycol is another factor that influences the velocity of the oxidation. We investigated the oxidation of two stereoisomers: symm. diphenyl-p-ditolylbutinediol (m.p. 132-133° and 144-146°) and symm. dimethyldiphenylbutinediol (m.p. 123-125° and 163-165°). It appeared that the low-melting isomer of symm. dimethyl-p-ditolylbutinediol was oxidized to the extent of 74% at 50° in 8 hours (average of 6 expts.); under the same conditions, the high-melting isomer was oxidized to the extent of 32.5% in 5 hours (average of 4 expts.). No addition oxidation was observed upon further heating.

We obtained similar results in the oxidation of symm. dimethyldiphenylbutinediol. The glycol with m.p. 123-125° was 78% oxidized after 5 hours at 80° (average of 5 expts.); under the same conditions, the glycol with m.p. 163-165° was 47% oxidized after 3 hours (average of 6 expts.).

The differences in the velocity of oxidation of optical isomers can apparently be explained by the degree of polarization of the molecule. From the experimental data we can draw the conclusion that the greater the polarization of the molecule, the more rapidly acetylation takes place. If we assume that the low-melting glycols are the l-isomers, and the high-melting glycols the d + l isomers, then the structure of the molecule may be indicated in the following diagram:


(I)


(II)

The degree of polarization of the molecule must be greater in the case of the i-isomers (I), in analogy with cis-compounds, than with the trans isomers (II).

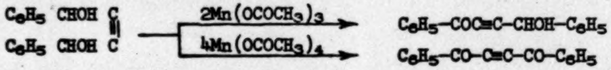
The different behaviors of stereoisomeric glycols were observed by Yu.S. Zalkind [8] in an investigation of the kinetics of hydrogenation of γ-acetylene glycols in the presence of colloid Pd. For example, the stereoisomeric symmetrical dimethyldiphenylbutinediols with m.p. 125-127° and 163° were hydrogenated at different speeds. While the isomer with m.p. 125-127° adds 2 atoms of hydrogen in 1 hour and 40 minutes, under the same conditions the isomer with m.p. 163° adds 2 atoms of hydrogen in 6 hours.

EXPERIMENTAL

The oxidation of diphenylbutinediol

$$C_6H_5—CHOH—C\equiv C—CHOH—C_6H_5$$

The glycol was synthesized by the usual method from dimagnesiumdibromoacetylene and benzaldehyde. The oxidation was carried out with the aim of obtaining the ketoalcohol and the diketone:



$$\begin{matrix} C_6H_5\ CHOH\ C \\ \| \\ C_6H_5\ CHOH\ C \end{matrix} \;\begin{matrix} \xrightarrow{2Mn(OCOCH_3)_3} & C_6H_5-COC\equiv C-CHOH-C_6H_5 \\ \xrightarrow{4Mn(OCOCH_3)_4} & C_6H_5-CO-C\equiv C-CO-C_6H_5 \end{matrix}$$

For the first experiment, the ratio 1:2 was used. 0.24 g of glycol with m.p. 137-138°, 0.70 g of 68.5% manganese triacetate, and 100 ml of chemically pure glacial acetic acid were used.

After each hour, a sample was taken for the determination of the percent of manganese triacetate contained in the acetic acid solution.

For the second experiment, the ratio 1:4 was used. 0.48 g of glycol with m.p. 137-138°, 2.80 g of 68.5% manganese triacetate, and 100 ml of chemically pure glacial acetic acid were used.

At a temperature of 50°, the glycol was 25% oxidized; at 80°, 83%; at 100°, 98%.

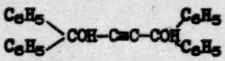
In order to investigate the products of oxidation, we carried out experiments with a 1:4 ratio. We shall describe one of the experiments.

1.0 g of glycol with m.p. 137-138°, 4.5 g of 84% manganese triacetate, and 100 ml of glacial acetic acid were used.

The oxidation was carried out completely at 100°. At the end of the reaction, which we could detect by the decolorization of the solution, part of the acetic acid (75 ml) was distilled off. The rest of the solution was poured into 100 ml of water. A viscous oily red liquid separated. This hardened upon standing. The precipitate was filtered off, washed with water to remove acetic acid, and recrystallized from alcohol. The alcoholic solution gave an amorphous precipitate with a reddish color. 0.58 g was obtained with m.p. 110.5-112°.

According to the data in the literature, the melting point of diphenylbutinedione is 111° [9].

The oxidation of tetraphenylbutinediol



$$\begin{matrix} C_6H_5 \\ C_6H_5 \end{matrix}\!\!>COH-C\equiv C-COH<\!\!\begin{matrix} C_6H_5 \\ C_6H_5 \end{matrix}$$

In contradistinction to diphenylbutinediol, tetraphenylbutinediol was oxidized only at 80°, to the extent of 87%.

In order to investigate the products of oxidation, experiments were carried out with 0.01 mole of the glycol.

3.9 g of glycol with m.p. 198-198.5°, 7.0 g of 68.5% manganese triacetate, and 100 ml of glacial acetic acid were used.

At the end of the reaction, part of the acetic acid was driven off (75 ml).

The rest of the solution was diluted with 100 ml of water. This gave 3.2 g of a yellow amorphous precipitate, which dissolved with difficulty in boiling alcohol, and was more soluble in boiling acetic acid. The alcohol gave a precipitate of golden crystals with m.p. 189-190°; the crystals from acetic acid melted at 189.5-191°.

The mother alcoholic liquor (after precipitation of the crystals with m.p 189-190°) gave a precipitate with a clear yellow color (0.4 g) with m.p. 115-150°. The rest of the filtrate (after the removal of the substance with m.p. 115-150°) was diluted with water. This gave a yellow oily precipitate (0.2 g) which hardened when seeded with tiny benzophenone crystals. M.p. 48-49°. A mixed test with benzophenone gave no melting point lowering.

Analysis of the crystalline substance with m.p. 189-190°:

0.1287 g substance: 0.3694 g CO_2; 0.0602 g H_2O.
0.2060 g substance: 22.90 g benzene: $\Delta t = 0.096°$.
Found %: C 78.28; H 5.20; M 475.1.
$C_{32}H_{26}O_5$. Computed %: C 78.37; H 5.31; M 490.

Determination of active hydrogen:

0.0773 g substance: 1.1 ml CH_4 (13°, 763 mm).
$C_{32}H_{26}O_4(OH)_2$. Computed: 11.4 ml CH_4.

The analysis showed the absence of hydroxyl groups.

Determination of acetyl groups.

The acetyl groups present were determined by saponifying a sample of the substance with an alcoholic solution of caustic potash. At the end of the saponification, the excess alkali was titrated with sulfuric acid.

0.1208 g substance; 5 ml KOH (T = 0.020637).
The titration required 12.95 ml H_2SO_4 (T = 0.005145).
Found %: $(OCOCH_3)_2$ 23.45.
$C_{28}H_{20}O(OCOCH_3)_2$. Computed %: $(OCOCH_3)_2$ 24.08.

After saponification of the diacetate, the reaction mixture was distilled with steam. This left in the distilling flask a crystalline substance with m.p. 161-163°, which has not as yet been more closely investigated.

The synthesis of p-tetratolylbutinediol

$$(CH_3C_6H_4)_2COH{-}C{\equiv}C{-}COH(C_6H_4CH_3)_2$$

We obtained the glycol from dimagnesiumdibromoacetylene and p-ditolylketone. The ditolylketone was synthesized from ditolylmethane.

The literature indicates that ditolylmethane is obtained by the condensation of toluene with formalin in the presence of sulfuric acid, in yields of 15 to 20% [10]. We were unable to obtain ditolymethane by this method, the chief product of the condensation being an amorphous substance which did not distil in a vacuum of 3 to 4 mm and was insoluble in the usual solvents. Therefore we used the method of A.M.Nastyukov, with several modifications. We carried out the reaction with cooling in the presence of a small quantity of sulfuric acid and with an alcoholic solution of formalin.

We shall give a description of one of our experiments. To 38 ml of (37%) formalin, diluted with 15 ml of alcohol, during stirring and cooling, there were added drop by drop 75 ml of concentrated sulfuric acid and then 200 ml of toluene. After all the toluene had been added, the reaction mixture was stirred for from 6 to 7 hours at a temperature of 40-50°. The contents of the flask were then poured into a separatory funnel. The upper, toluene, layer was removed from the sulfuric acid, dried over potash, and distilled over metallic sodium to give 3 fractions:

1st fraction:	100°	3 g,
2nd fraction:	118-120°	20 g,
3rd fraction:	284-286°	100 g.

The third fraction was distilled twice at 3 mm pressure. We obtained 85 g of a substance with b.p. 128-130°. The yield was 50%, computed on the amount of toluene consumed.

We obtained p-ditolylketone by oxidizing p-ditolylmethane with nitric acid. The method describing the preparation of m- and p-ditolylketone by oxidation with CrO_3 in glacial acetic acid [8] gave very low yields.

We shall describe one of our experiments. 5 g of ditolylmethane, 12 ml of water, and 0.5 g of lead acetate were heated to the boiling point. While the boiling solution was stirred mechanically, 40 ml of nitric acid (sp. gr. 1.4) was added. The reaction was accompanied by a voluminous evolution of nitrogen oxides. The heating was continued until no more nitrogen oxides were evolved. At the end of the reaction, the mixture was poured into cold water, and an oily, viscous yellow liquid separated out. This hardened upon cooling. Crystallization from methyl alcohol gave needle-shaped crystals of a light-yellow color, with m.p. 90-92°. Yield 18 g, or 30%. In addition to the ketone, we obtained crystals with m.p. 150-152°. These were not investigated further.

For the synthesis of the glycol, p-tetratolylbutinediol, we first prepared, according to the directions of Yotsich, dimagnesiumdibromoacetylene. Then we added the ketone under conditions somewhat different from those described by G. A. Arbuzov and his coworkers [11]. We poured in a benzene solution of p-ditolylketone which contained 50% of the amount of ketone theoretically needed. After the ketone had all been added, the reaction mixture was stirred for 6 days while being heated on the water bath, and the glycolate was then decomposed with a concentrated solution of ammonium sulfate. The ether-benzene solution was dried over calcined sodium sulfate. The solvent was then distilled off to leave a thick, viscous mass, which was washed with petroleum ether. After treatment with petroleum ether, there remained an oily liquid which soon hardened. Two recrystallizations from ligroin gave needle-shaped crystals with m.p. 135-136°. The 100-120° fraction crystallized from benzene with m.p. 136.5-137.5°. Yield 70%, based on the amount of ketone used.

With concentrated sulfuric acid, the glycol gives a cherry-red color (p-ditolylketone gives a brown color with sulfuric acid). The glycol we obtained did not react with an ammoniacal solution of silver oxide or with cupric chloride; therefore, the compound did not correspond to the composition of p-ditolylacetylenylcarbinol. A test for the presence of a triple bond by heating with sodium in amyl alcohol gave a positive result.

The oxidation of p-tetratolylbutinediol

We shall describe one of the oxidation experiments. 0.223 g of the glycol with m.p. 136.5-137.5° , 0.412 g of 54% manganese triacetate, and 50 ml of glacial acetic acid were used. If the oxidation is carried out at 80°, the reaction is complete after an hour, the amount of manganese acetate used up in the first 15 minutes amounting to 50%.

In order to investigate the products obtained by oxidation, we carried out larger-scale experiments. In order to avoid secondary reactions, which might take place during the driving off of the solvent, the acetic acid solution, at the end of the oxidation, was poured into water. This gave a yellow precipitate which was very soluble in benzene, petroleum ether, and acetic acid, and not so soluble in methyl and ethyl alcohol. The methyl alcohol solution gave crystals of a clear-yellow color, with m.p. 85-87°. With concentrated sulfuric acid, the crystals gave a cherry-red color. A mixed test with p-ditolylketone gave an unsharp melting range of 76-88°.

Determination of the molecular weight by the cryoscopic method in benzene:

0.1728 g substance: 21.69 g C_6H_6: Δt 0.077°.
Found: M 525.5.
$C_{36}H_{34}O_5$. Computed: M 546.0.

Elementary analysis:

0.1761 g substance: 0.5152 g CO_2; 0.1059 g H_2O.
Found %: C 79.79; H 6.64.
$C_{36}H_{34}O_5$. Computed %: C 79.12; H 6.41.

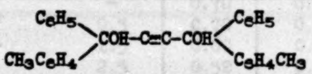
Determination of acetyl groups.

0.1636 g substance: 5 ml KOH (T = 0.01922).
The back-titration required 13.3 ml of H_2SO_4 (T = 0.004530).
Found %: $(OCOCH_3)_2$, 22.17.
$C_{32}H_{28}O(OCOCH_3)_2$. Computed %: $(OCOCH_3)_2$ 21.67.

Tests for the presence of triple bonds, carbonyl groups, and active hydrogen gave negative results.

An acetone solution of potassium permanganate and an acetic acid solution of bromine were not decolorized. On the basis of these reactions, we can ascribe to the compound obtained the structure 2,2,5,5-tetratolyl-3,4-diacetyldihydrofuran-3,4.

The synthesis and oxidation of symm. diphenyl-p-ditolylbutinediol.



$$\begin{matrix} C_6H_5 & & C_6H_5 \\ & COH-C\equiv C-COH & \\ CH_3C_6H_4 & & C_6H_4CH_3 \end{matrix}$$

We synthesized the glycol from dimagnesiumdibromoacetylene and phenyltolylketone. The phenyltolylketone was obtained by the Friedel-Crafts reaction in 70% yield. Two recrystallizations from petroleum ether gave colorless crystals in the form of little needles, with m.p. 54.5-55.5°.

The glycol was synthesized by the method described by Yu.S.Zalkind and E.E. Martinson [12]. But, in contradistinction to the authors, we used for this reaction 40% of the theoretical amount of ketone, and we carried out the decomposition of the glycolate with a concentrated solution of ammonium sulfate. After removal of the volatile products with steam and numerous recrystallizations from ligroin gasoline, we obtained two fractions: m.p. 132-134° (chief product of the reaction) and 144-146° (very small quantity). A mixed test of both fractions gave an unsharp melting range of 128-136°. According to the data of Yu.S.Zalkind, the melting point of the glycol is 146°.

Determination of the molecular weight of the glycol with m.p. 132-134°, cryoscopically in benzene:

0.3718 g substance: 23.44 g C_6H_6: Δt 0.195°.
Found: M 413.8.
$C_{30}H_{26}O_2$. Computed: M 418.1.

Elementary analysis:

0.1541 g substance: 0.4841 g CO_2; 0.0911 g H_2O.
Found %: C 85.88; H 6.30.
$C_{30}H_{26}O_2$. Computed %: C 86.13; H 6.20.

Determination of the molecular weight of the glycol with m.p. 144-146°, cryoscopically in benzene:

0.2308 g substance: 23.11 g C_6H_6: Δt 0.118°.
Found: M 429.1.
$C_{30}H_{26}O_2$. Computed: M 418.1.

Elementary analysis:

0.1216 g substance: 0.3851 g CO_2; 0.0707 g H_2O.
Found %: C 86.35; H 6.46.
$C_{30}H_{26}O_2$. Computed %: C 86.13; H 6.20.

The oxidation of the diphenyl-p-ditolylbutinediol with m.p. 132-134°.

We shall describe one of the oxidation experiments at 50 and at 80°, carried out on the glycol with m.p. 132-134°.

We used 0.209 g of glycol (1/2000th mole), 0.8 g of 27% $Mn(OCOCH_3)_3$ (0.001 mole), and 50 ml of glacial acetic acid.

Table 1

Velocity of oxidation at 50°.

Activity of the solution at 20° before the addition of glycol, 0.56 ml; after the addition of glycol, 0.53 ml

Duration of heating, hrs.	Amount $Na_2S_2O_3$, ml	$Mn(OCOCH_3)_3$ %
0.5	0.52	0.427
1.0	0.46	0.380
2.0	0.38	0.310
3.0	0.33	0.270
5.0	0.20	0.164
7.0	0.17	0.140
		77% oxidized

Activity of the solution at 20° before the addition of glycol 0.64 ml, after the addition of glycol 0.62 ml

0.5	0.20	0.144
1.0	0.12	0.086
1.5	0.06	0.36
		92% oxidized

Table 2

Velocity of oxidation

Duration of heating, hrs.	Amount of $Na_2S_2O_3$, ml	$Mn(OCOCH_3)_3$, %	Note
-	0.70	0.460	
0.5	0.70	0.460	
1.5	0.60	0.394	
2.5	0.52	0.342	
3.5	0.48	0.315	
4.5	0.48	0.315	32% oxidized
-	0.49	0.315	
5.0	0.38	0.250	
6.0	0.20	0.131	
7.0	0.16	0.105	
8.0	0.10	0.067	85% oxidized

The oxidation of Symm. Diphenylditolylbutinediol with m.p. 144-146°.

The conditions of reaction were the same as in the previous experiments.

0.209 g of the glycol (1/2000th mole), 0.326 g 71.6% $Mn(OCOCH_3)_3$ (0.001 mole), and 50 ml of glacial acetic acid were used.

In order to investigate the structure of the compounds obtained by oxidation, we ran larger scale experiments, carried out in the same way as the previous experiments. Crystallization from methyl alcohol gave yellow-colored crystals with m.p. 80-82°.

Determination of molecular weight cryoscopically in benzene:

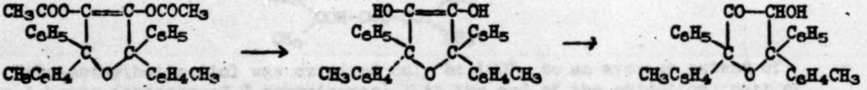
0.1594 g substance: 23.47 g C_6H_6: Δt 0.069°.
Found: M 499.9.
$C_{34}H_{30}O_5$. Computed: M 518.0.

Elementary analysis:

0.03337 g substance: 0.9682 g CO_2; 0.1656 g H_2O.
Found %: C 79.13; H 5.66.
$C_{34}H_{30}O_5$. Computed %: C 78.76; H 5.79.

Saponification of the diacetate with m.p. 80-82°.
1.0498 g substance: 10 ml KCH (T 0.04714).
A back titration required 51.3 ml H_2SO_4 (T 0.004235).
Found %: $(OCOCH_3)_2$ 22.40.
Computed %: $(OCOCH_3)_2$ 22.86.

By means of saponification, a cyclic ketoalcohol of the following structure should have been obtained:



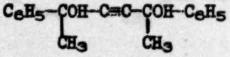
In order to determine the structure resulting from saponification, the ether extract was removed. It was dried over calcined sodium sulfate and the ether driven off to leave a viscous, colored liquid which did not crystallize on standing. The oily material was therefore treated with semicarbazide in the usual way to give a semicarbazone. This melted at 251-252° with decomposition. In a sealed capillary, the m.p. was 245-246°, with decomposition.

Determination of nitrogen:

0.1624 g substance: 12.4 ml N_2 (22°, 766.5 mm).
Found %: N 8.70.
$C_{31}H_{29}O_3N_3$. Computed %: N 8.55.

On the basis of the reactions carried out, we may ascribe to the oxidation product of symm.diphenyl-p-ditolylbutinediol the structure 2,5-diphenyl-2,5-p-ditolyl-3,4-diacetyldihydrofuran.

The oxidation of symm. dimethyldiphenylbutinediol



$$C_6H_5-\underset{\displaystyle CH_3}{\underset{|}{C}}OH-C{\equiv}C-\underset{\displaystyle CH_3}{\underset{|}{C}}OH-C_6H_5$$

The glycol was synthesized by the usual method from acetophenone and dimagnesiumdibromoacetylene. Numerous crystallizations from ligroin gave two products with m.p. 123-125° and 163-164.5°.

We shall describe the results of one of the experiments on the oxidation of the glycol with m.p. 123-125° and one with 163-164.5°.

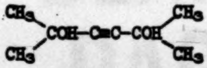
We used 0.133 g of glycol (1/2000th mole), 0.300 g of 83% $Mn(OCOCH_3)_3$ (0.001 mole), and 50 ml of acetic acid.

TABLE 3

Velocity of the oxidation of the glycol with m.p. 123-125° (experiment 1) and with m.p. 163-164.5° (experiment 2)

Experiment No.	Temperature, °	Time, hours	Amount of $Na_2S_2O_3$, in ml	$Mn(OCOCH_3)_3$, %	Note
1	50	-	0.72	0.460	
		1	0.77	0.460	
	80	2	0.57	0.340	
		3	0.30	0.180	
		4	0.16	0.095	
		5	0.16	0.095	78% oxidized
2	80	-	0.76	0.460	
		1	0.65	0.380	
		2	0.48	0.280	
		2	0.45	0.260	43% oxidized

The oxidation of tetramethylbutinediol

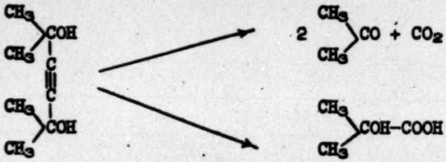


$(CH_3)_2COH{-}C{\equiv}C{-}COH(CH_3)_2$

Tetramethylbutinediol was oxidized only at 100°, to an average extent of 43% in 3 hours (average of 7 experiments). At the end of the oxidation, part of the acetic acid was driven off. Acetone was detected in the acetic acid by means of a sodium nitroprusside test. After the usual treatment of the oxidation products and extraction with ether, a crystalline product with m.p. 80° was obtained. This had acid properties (test with Na_2CO_3).

A mixed test with tetramethylbutinediol gave an unsharp melting range of 63-80°. According to the data in the literature, the melting point of α-hydroxyisobutyric acid is 79°. No oxalic acid was detected in the aqueous solution.

On the basis of the experiments which were carried out, the mechanism of the oxidation can be pictured in the following manner:



SUMMARY

1. Secondary γ-acetylene glycols (diphenylbutinediol) react with manganese triacetate to give γ-diketones of the acetylene series.

2. It has been shown that manganese triacetate acts as an acetylating agent at the triple bond only with tertiary γ-acetylene glycols of the aromatic series, in this way giving diacetyl derivatives of the dihydrofuran series.

3. γ-Acetylene glycols of the alkyl series are oxidized in a way to break up the carbon skeleton.

4. The stereoisomeric structure of the glycols, in addition to the character of the radicals, influences the velocity of the reaction.

5. The glycols which have been investigated may be arranged in the following order with regard to velocity of oxidation: p-tetratolyl-, symm. diphenyl-p-ditolyl-, tetraphenyl-, and tetramethylbutinediol.

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ON THE HYDRAZONES OF α,γ DIPHENYL ACETOACETIC ESTER

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In the course of our work on the synthesis of the alkaloids of the celandine Chelidonium majus and of benzophenanthridene compounds which might serve as a model for the chelidonium molecule, we became interested in the preparation of various α,γ-diphenylbutyric acids, which contained a substituent in the β-position. In particular, it seemed of definite interest to obtain β-amino-α,γ-diphenylbutyric acid, which is also related to the intensive work on the investigation of β-amino acids carried on in our laboratory. We attempted to obtain this β-amino acid by the reduction of the phenyl hydrazone of α,γ-diphenylacetoacetic ester, as α,γ-diphenylacetoacetic ester is easily obtained by the condensation of phenylacetic ester under the action of isopropylmagnesium bromide [1].

The reduction of the phenylhydrazones of keto acids to give the corresponding amino acids has been very thoroughly studied. Here, in the first place, we must mention the brilliant work of V.V.Feofilaktov [2], who obtained a large number of α-amino acids by the reduction of the phenylhydrazones of α-keto acids, the latter being easily obtained by the action of phenyldiazonium chloride on alkylacetoacetic esters. This reduction was carried out by the action of zinc dust and an alcoholic solution of hydrogen chloride on the alcoholic solution of the phenylhydrazone itself, and took place almost quantitatively.

Another frequently used reagent for the reduction of phenylhydrazones of keto acids to amino acids is aluminum amalgam. Using this, E.Fischer and Groh [3] obtained γ-aminovaleric acid, β-aminobutyric acid, and alanine by the reduction of the phenylhydrazones of the corresponding acids in yields which averaged about 60%. By the reduction of acylated hydrazones of β-keto acids by means of aluminum amalgam, Decombe [4] obtained the esters of β-aminobutyric, β-aminocaproic, and β-aminocaprylic acids.

Tafel [5] reduced the phenylhydrazones of keto acids with sodium amalgam, but the use of the latter gave worse results than aluminum amalgam, because of the great difficulty of separating the amino acids which were formed.

In our work on the reduction of the hydrazones of α,γ-diphenylacetoacetic esters we encountered a rather peculiar form of behavior of these compounds. This, in fact, is the subject of the present article.

The phenylhydrazones of α,γ-diphenylacetoacetic ester are not described in the literature. Volhard [6] added a hot solution of α,γ-diphenylacetoacetic ester in glacial acetic acid to an acetic solution of phenylhydrazine to obtain 1,4-diphenyl-3-benzyl-5-pyrazolone, with m.p. 231-232°, in 92% yield. This same pyrazolone was obtained by Walther and Schickler [7] by heating the amide of α,γ-diphenylacetoacetic ester in glacial acetic acid with an acetic acid solution of phenylhydrazine. According to their data, it melted at 228°.

It appeared possible that if the reaction between α,γ-diphenylacetoacetic ester and phenylhydrazine were carried out at room temperature, it would be possible to stop it at the phenylhydrazone stage, and to avoid closure of the ring such as took place when acetoacetic ester was made to react with phenylhydrazine [e].

Experiment did not confirm these expectations. If α,γ-diphenylacetoacetic ester is mixed with an excess of phenylhydrazine and benzene is added until the keto ester has completely dissolved, no obvious evolution of heat takes place, but after an hour and a half the reaction mixture begins to crystallize. After a day, the reaction product was squeezed out on a filter and carefully washed with alcohol, then dried in a vacuum desiccator at room temperature. The substance was not recrystallized in order to avoid ring-formation. A determination of its melting point (229-231°) showed that the product obtained was a pyrazolone derivative, and not the phenylhydrazone. Taking into consideration the possibility that ring formation of the phenylhydrazone of α,γ-diphenylacetoacetic ester might have occurred in the capillary during the determination of the melting point, we carried out a complete analysis of the compound we had obtained. This clearly showed that it was 1,4-diphenyl-3-benzyl-5-pyrazolone, and that ring closure took place even at room temperature, at which this pyrazolone was formed in a yield of 80.6% of the analytically pure product.

Inasmuch as it proved impossible to obtain the phenylhydrazone of α,γ-diphenylacetoacetic ester, it was decided to obtain the methylphenylhydrazone, which was not capable of giving a pyrazolone derivative. In contrast to the reaction of phenylhydrazine with α,γ-diphenylacetoacetic ester, the reaction of the latter with asymm. methylphenylhydrazine did not take place at room temperature. Even when the α,γ-diphenylacetoacetic ester was boiled with a 10% molar excess of this reagent in alcohol for 5 hours, the α,γ-diphenylacetoacetic ester could be recovered almost quantitatively. Only when a large excess of asymm. methylphenylhydrazine was used, and it was heated with α,γ-diphenylacetoacetic ester on the boiling water bath for several hours was it possible to obtain the methylphenylhydrazone of α,γ-diphenylacetoacetic ester in good yield (50 to 65%). After recrystallization from methyl alcohol, it had m.p. 90.5 to 91.5°, and a composition which corresponded to that required for this compound.

Volhard [e], in his attempts to obtain the oxime of α,γ-diphenylacetoacetic ester, encountered similar difficulties in the formation of the usual derivatives attached to the carbonyl group of this compound. Upon heating α,γ-diphenylacetoacetic ester with hydroxylamine in aqueous-alcohol solution in open vessels, the keto ester was recovered from the reaction in unaltered form. The reaction took place only upon heating in sealed tubes, to give a mixture of the oxime of α,γ-diphenylacetoacetic ester and 4-phenyl-3-benzyl-5-isoxazolone. The latter was formed to a predominant degree.

This difficulty of preparation of the normal carbonyl derivatives (the methylphenylhydrazone), and at the same time the remarkable ease of formation of the pyrazolone derivative during the reaction of α,γ-diphenylacetoacetic ester with phenylhydrazine forced us to doubt the correctness of Volhard's results [e] on the reaction between these keto esters and hydrazine hydrate.

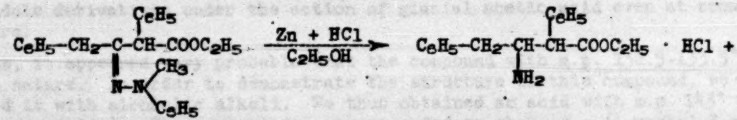
Upon heating 5 parts of α,γ-diphenylacetoacetic ester with one part of hydrazine hydrate and 8 parts of alcohol on the water bath for an hour, Volhard obtained a product which after recrystallization from alcohol melted at 125-126°. Inasmuch as this substance had approximately the composition of the hydrazone of α,γ-diphenylacetoacetic ester (however, in his paper the author does not give the data of his analysis) Volhard, without any additional investigation, ascribed this structure to it. After recrystallization from toluene, the melting point of this compound rose to 137-141°, and a subsequent recrystallization from alcohol gave a product with m.p. 172°. After drying at 125°, this lost a molecule of alcohol of crystallization, and then corresponded to the composition of 4-phenyl-3-benzyl-5-pyrazolone.

It appeared to us, however, that ring formation might take place even during the boiling in alcohol, and that Volhard's hydrazone might be the considerably contaminated pyrazolone derivative. Repeating Volhard's experiment accurately, we actually obtained, by means of heating a mixture of α,γ-diphenylacetoacetic ester, hydrazine hydrate, and alcohol on the water bath for an hour in the ratios indicated above, a product which melted, after recrystallization from alcohol and drying in a vacuum desiccator, at 126-127°.

When we carried out a complete analysis of this substance, however, it was seen that its composition was much closer to that of the pyrazolone derivative than to that of the hydrazone. In addition, this substance dissolved in alkali and was precipitated by acetic acid. This showed without any doubt the pyrazolone nature of this compound. If the substance with m.p. 126-127° was dried in a desiccator at a temperature of 60-70°, or recrystallized from a solvent which boiled not far from the boiling point of alcohol, like benzene or chloroform (in order to avoid possible ring formation during recrystallization) then its melting point rose sharply (to 152-155°). However, the substance could be purified by recrystallization from these solvents only with difficulty.

The most suitable method of purification of this compound was its solution in alkali and precipitation with acetic acid. This at once gave a compound with m.p. 171-172°. After recrystallization from alcohol, and drying at a temperature of 120° for 7 hours, this melted at 172.5-173°, and had a composition corresponding to that of 4-phenyl-3-benzyl-5-pyrazolone. Thus, we had to accept the conclusion that Volhard did not succeed in isolating the hydrazone of α,γ-diphenylacetoacetic ester, as an intermediate stage in the formation of this pyrazolone derivative.[*]

Having obtained the methylphenylhydrazone of α,γ-diphenylacetoacetic ester, we tried to reduce it by Feofilaktov's method, i.e., by the action of zinc dust and an alcoholic solution of hydrogen chloride, while the compound was cooled with ice water. We expected to obtain in this way two compounds with a basic character, the ethyl ester of β-amino-α,γ-diphenylbutyric acid, and monomethylaniline:



$$C_6H_5{-}CH_2{-}\underset{\underset{N{-}N(CH_3)C_6H_5}{\|}}{C}{-}\overset{\overset{C_6H_5}{|}}{C}H{-}COOC_2H_5 \xrightarrow[C_2H_5OH]{Zn + HCl} C_6H_5{-}CH_2{-}\underset{\underset{NH_2}{|}}{C}H{-}\overset{\overset{C_6H_5}{|}}{C}H{-}COOC_2H_5 \cdot HCl + C_6H_5NHCH_3 \cdot HCl.$$

The formation in 87% yield of a neutral substance with m.p. 132.5-133.5° (from CH_3OH), and of only insignificant traces of the bases, was completely unexpected. This substance was also formed when the methylphenylhydrazone of α,γ-diphenylacetoacetic ester was treated under the same conditions as in the first case, but without zinc dust. The formation of this compound was also noted when the methylphenylhydrazone was heated in glacial acetic acid, or when the latter was used as a solvent for the synthesis of this hydrazone. As far as composition went, the substance with m.p. 132.5-133.5° corresponded to a product of Fischer's indole synthesis – the ethyl ester of α-(1-methyl-3-phenyl-2-indolyl)-phenylacetic acid, whose formation may be expressed by the equation:

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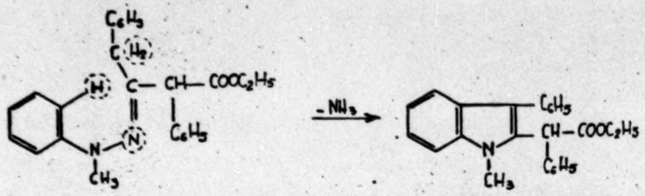
[*] We must note the interesting fact that the determination of nitrogen by Dumas' method in this compound just as with the indole derivatives which are related to it gives high results despite the good analysis for carbon and hydrogen. The determination of nitrogen by a micro Kjeldahl method gives excellent results.



As a rule, the formation of indoles from phenylhydrazines takes place under rather harsh conditions: heating with anhydrous $ZnCl_2$ or Cu_2Cl_2 at a temperature of the order of 160 to 180°, or heating with mineral acids. However, a number of cases are given in the literature where arylhydrazones easily rearrange to give the corresponding indole derivatives.

Thus, for example, Perkin [9] heated the phenylhydrazone of cyclohexanone in glacial acetic acid to obtain tetrahydrocarbazole. Walker [10] observed the formation of the ethyl ester of α-(α-indolyl)-propionic acid when the phenylhydrazone of α-methylacetoacetic ester was treated at a temperature of -15° with concentrated sulfuric acid; this example is interesting because here the rearrangement to give an indole derivative takes place more easily than ring formation to give a pyrazolone compound.

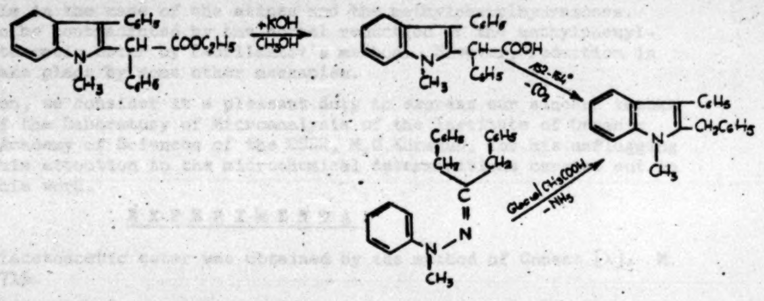
Hughes and his coworkers [11] carried out the transformation of the phenylhydrazones of α-keto acids into substituted indoles by passing dry HCl into their solutions in absolute alcohol.

Feofilaktov [12] carried out ring-formation in similar hydrazones by heating them in alcohol in the presence of H_2SO_4.

Closest to our own example is the work of Neber and his coworkers [13], who showed that N-alkyl (aryl)-phenylhydrazones of carbonyl compounds which had atoms of hydrogen on the methylene group, necessary for the splitting off of ammonia, under the influence of neighboring phenyl or carbonyl groups (for example, the hydrazones of methylbenzylketone, dibenzylketone, or α-nitrophenylpyruvic acid) formed indole derivatives under the action of glacial acetic acid even at room temperature.

Thus, it appeared very probable that the compound with m.p. 132.5-133.5° had an indole nature. In order to demonstrate the structure of this compound, we saponified it with alcoholic alkali. We thus obtained an acid with m.p. 143° (with decomposition). Its composition corresponded to that of α-(1-methyl-3-phenyl-2-indolyl)-phenylacetic acid. When this acid was heated to a temperature of 152-154°, it easily lost a molecule of CO_2, and was converted into 1-methyl-2-benzyl-3-phenylindole, identical with that obtained by Neber [13] from the methylphenylhydrazone of dibenzylketone (cf. formula on p. 1332). This conclusively showed the structure of the substance with m.p. 132.5-133.5° to be that of an ethyl ester of α-(1-methyl-3-phenyl-2-indolyl)-phenylacetic acid.

We must note one more very curious circumstance. When we were developing the method of preparation of the methylphenylhydrazone of α,γ-diphenylacetoacetic ester, in one of the experiments in which asymm. methylphenylhydrazine was heated with α,γ-diphenylacetoacetic ester in glacial acetic acid, we obtained a compound which melted, after purification, at 103-104°, and had a composition and properties completely identical with those of the indole derivative with m.p. 132.5-133.5°. Upon saponification, both these compounds gave one and the same acid, but the lower-melting compound crystallized with considerable more difficulty than the higher melting one. Upon standing, the melting point rose to 132-133°. Once we were able to observe that this compound melted at 102.5-103.5°, then solidified, and melted again at 132-133°.



We could not repeat this observation, despite numerous attempts. After we had obtained the high-melting compound in our laboratory, we were never again able to obtain the indole derivative with m.p. 103-104°. Despite the fact that we endeavored to reproduce accurately the conditions of the earlier experiments, we always obtained the high-melting compound, which crystallized very easily, while the product with m.p. 103-104° precipitated in the form of an oil, and crystallized only after rubbing with cold methyl alcohol. Probably these two substances are polymorphic forms.

Neber [13] observed a similar phenomenon with the oxime of 1-methyl-2-benzoyl-3-phenylindole, which was obtained in the form of pale yellow needles with m. p. 165°. Upon standing, the color of the oxime became deeper, and after recrystallization from alcohol it melted at 195°, while its analytical composition was not at all changed. We must note, however, that in this case, syn-anti isomerism is possible, and that it was not possible in our example. But here too it is more likely that we have polymorphism.

Thus, instead of the normal reduction of the methylphenylhydrazone of α,γ-diphenylacetoacetic ester under the conditions of reduction by the Feofilaktov method, there takes place a rearrangement to give an indole derivative. Wishing to learn whether this behavior is a general property of the methylphenylhydrazones of β-keto esters, we obtained, by Degen's method [14], the methylphenylhydrazone of acetoacetic ester. A preliminary experiment on its reduction with zinc dust and an alcoholic solution of hydrogen chloride gave a negative response: upon reduction it was possible to obtain only negligible amounts of the neutral product. The normal product of reduction was obtained, monomethylaniline, characterized by the formation of its acetyl derivative with m.p. 100-101°, identical with that of a synthetic sample. We did not attempt to isolate the second product of the reaction, the ethyl ester of β-aminobutyric acid, because of the difficulty of obtaining this. This experiment showed that in the case in question reduction apparently takes place normally, and that the ease of transformation of the methylphenylhydrazone of the α,γ-diphenylacetoacetic ester into an indole derivative depends on the activating influence of the phenyl groups.

As we wished to avoid this rearrangement, we attempted to reduce this hydrazone with aluminum amalgam. In all our experiments, we recovered this compound in unchanged form almost quantitatively from the reaction. This fact must, apparently, be explained by steric hindrance. Decombe's [4] claim that in contrast to the phenylhydrazones and acyl hydrazones of β-keto acids, the azines of these compounds were not reduced by aluminum amalgam also deserves some attention. Perhaps this is related to the fact that the breaking of the N-N bond takes place through the intermediate formation of an azo form by means of the tautomeric transformation:

$$>C{=}N{-}NH{-}R \rightleftarrows >CH{-}N{=}N{-}R,$$

which is impossible in the case of the azines and the methylphenylhydrazones. This would seem to be contradicted by the normal reduction of the methylphenylhydrazones of acetoacetic ester by Feofilaktov's method. However, reduction in acid medium may take place by some other mechanism.

In conclusion, we consider it a pleasant duty to express our sincere thanks to the Director of the Laboratory of Microanalysis of the Institute of Organic Chemistry of the Academy of Sciences of the USSR, M.O.Korshun, for his unflagging interest and for his attention to the microchemical determinations carried out in connection with this work.

EXPERIMENTAL

α,γ-Diphenylacetoacetic ester was obtained by the method of Cnnant [1]. M. p. 76-77°; yield 71%.

1-4-Diphenyl-3-benzyl-5-pyrazolone

To a mixture of 0.70 g (0.0025 mole) of α,γ-diphenylacetoacetic ester and 1.00 g (0.01 mole) of phenylhydrazine, 1 ml of dry benzene was added to dissolve the keto ester completely. After an hour and a half, the reaction mixture crystallized. After a day, the crystals were filtered off with suction, carefully washed with alcohol, and dried in a vacuum desiccator at room temperature. 0.75 g of a substance with m.p. 229-231° was obtained. Yield 80.6%.

The literature gives for this compound: m.p. 231-232° [5]; 228° [7]; 229° [15].

The compound was analyzed without recrystallization:

Analysis for nitrogen:

3.210 mg substance: 0.243 ml N_2 (23°, 748 mm).
3.480 mg substance: 0.259 ml N_2 (25°, 748 mm).
Found %: N 8.59, 8.44.
$C_{22}H_{18}ON_2$. Computed %: N 8.58.

Analysis for C and H:

4.41 mg substance: 13.05 mg CO_2; 2.37 mg H_2O.
4.73 mg substance: 14.00 mg CO_2; 2.51 mg H_2O.
Found %: C 80.70, 80.72; H 6.01, 5.93.
$C_{22}H_{18}ON_2$. Computed %: C 80.94; H 5.56.

The methylphenylhydrazone of α,γ-diphenylacetoacetic ester

a) 0.80 g of the α,γ-diphenylacetoacetic ester, 0.37 g (10% molar excess) of asymm. methylphenylhydrazine, and 10 ml of alcohol were boiled on the water bath for 5 hours. The mixture was then allowed to stand overnight in the cold. The crystals which formed were filtered off with suction after additional cooling with a mixture of ice and salt, and they were washed with cold alcohol. We obtained 0.68 g of a material with m.p. 78-78.5°; this gave no lowering of the melting point when mixed with the original α,γ-diphenylacetoacetic ester.

b) 11.28 g (0.04 mole) of α,γ-diphenylacetoacetic ester was heated on the boiling water bath with 7.20 g (0.06 mole) of asymm. methylphenylhydrazine for 10 hours. The oil which formed was dissolved in hot methyl alcohol, to which was added 4 drops of glacial acetic acid. The amount of methyl alcohol was chosen to be just sufficient so that upon cooling the hydrazone did not precipitate in the form of an oil. Upon standing and rubbing with a glass stirring rod, a crystalline precipitate of the methylphenylhydrazone formed. The crystals were filtered off with suction and washed with cold methyl alcohol. The yield was 7.70 g, i.e., 49.7% of the theoretical. M.p. 89-90.5°. After recrystallization from methyl alcohol, the methylphenylhydrazone of α,γ-diphenylacetoacetic ester had m.p. 90.5-91.5°. It was soluble with difficulty in cold alcohol, soluble with ease in ether, chloroform, and benzene.. If this method is used with a 100% excess of methylphenylhydrazine, the yield of hydrazone rises to 66%.

Analysis for nitrogen:

4.499 mg substance: 2.32 ml 0.01 N H_2SO_4.
5.500 mg substance: 2.80 ml 0.01 N H_2SO_4.
Found %: N 7.22, 7.13.
$C_{25}H_{26}O_2N_2$. Computed %: N 7.25.

Analysis for C and H:

3.48 mg substance: 9.91 mg CO_2; 2.19 mg H_2O.
3.50 mg substance: 9.95 mg CO_2; 2.21 mg H_2O.
Found %: C 77.66, 77.53; H 7.04, 7.06.
$C_{25}H_{26}O_2N_2$. Computed %: C 77.70; H 6.78.

4-Phenyl-3-benzyl-5-pyrazolone

1.0 g of α,γ-diphenylacetoacetic ester, 0.2 g of hydrazine hydrate, and 1.6 g of alcohol were heated at the boiling point on the water bath for one hour. Upon cooling, the reaction mixture crystallized. It was cooled with ice, and the crystals filtered off with suction and washed with cold alcohol. The material was recrystallized from alcohol and dried in a vacuum desiccator. It sintered at 116°, and melted at 126-127°. As far as composition went, the material corresponded more nearly to 4-phenyl-3-benzyl-5-pyrazolone than to the hydrazone of α,γ-diphenylacetoacetic ester.

Analysis for nitrogen:

6.158 mg substance: 0.558 ml N_2 (21°, 727 mm).
6.195 mg substance: 0.561 ml N_2 (20°, 731 mm).
Found %: N 10.02, 10.15.
$C_{16}H_{14}ON_2$ (pyrazolone). Computed %: N 11.15.
$C_{18}H_{20}O_2N_2$ (hydrazone). Computed %: N 9.45.

Analysis for C and H:

3.02 mg substance: 8.43 mg CO_2; 1.30 mg H_2O.
3.56 mg substance: 9.95 mg CO_2; 1.55 mg H_2O.
Found %: C 76.13, 76.23; H 4.81, 4.87.
$C_{15}H_{14}ON_2$ (pyrazolone). Computed% C 76.79; H 5.64.
$C_{18}H_{20}O_2N_2$ (hydrazone). Computed %: C 72.94; H 6.80

The substance dissolved in alkali and was precipitated by acetic acid, in an excess of which it was soluble. It did not give the Bulow reaction, and reduced an ammoniacal solution of silver oxide only upon boiling.

After drying at 60° for several hours, this compound sintered at 130° and melted at 149°. After two recrystallizations from benzene, its melting point rose to 153-153.5°. This same melting point was acquired by the crude product after two recrystallizations from chloroform. Subsequent recrystallization from alcohol hardly raised the melting point. The best solvent for recrystallization was toluene, and recrystallization from this sometimes gave a melting point as high as 172°.

However, the toluene was firmly retained by the material, and even two days of drying in a desiccator at 70° did not free the substance from toluene. This was expressed in the results of analysis (a lowering of the nitrogen content, and an increase in the percent of carbon).

The best method for the purification of this compound was to dissolve it in a dilute solution of NaOH, to extract the alkaline solution three times with ether, and to precipitate the pyrazolone derivative with dilute acetic acid, until blue litmus began to turn red. By means of this method, the material was at once obtained with m.p. 171-172°.

After recrystallization from alcohol, the air-dried product melted at 172-172.5°. After drying at 120° for 7 hours (to remove alcohol of crystallization) the substance melted at 172.5-173°. According to the data of Volhard, 4-phenyl-3-benzylpyrazolone has m.p. 172°.

Analysis for nitrogen:

3.780 mg substance: 0.357 ml N_2 (24°, 744 mm).
Found %: N 10.63.
$C_{16}H_{14}ON_2$. Computed %: N 11.20.

Analysis for C and H:

3.50 mg substance: 9.87 mg CO_2; 1.61 mg H_2O.
3.62 mg substance: 10.22 mg CO_2; 1.73 mg H_2O.
Found %: C 76.91, 77.00; H 5.14, 5.34.
$C_{16}H_{14}ON_2$. Computed %: C 76.79; H 5.64.

The ethyl ester of α-(1-methyl-3-phenyl-2-indolyl)-phenylacetic acid

a) The reduction of the methylphenylhydrazone of α,γ-diphenylacetoacetic ester, by Feofilaktov's method. 1.00 g of the methylphenylhydrazone of α,γ-diphenylacetoacetic ester was dissolved in a mixture of 25 ml of glacial acetic acid and 10 ml of alcohol. The solution was stirred mechanically and cooled with ice water while 1 g of zinc dust was gradually added at the same time as an alcoholic solution of hydrogen chloride was added drop by drop. After some time, the formation of a precipitate was noted. The reduction was continued over a period of 7 hours. The precipitate was filtered with suction and washed with alcohol. 0.65 g of material was obtained. After recrystallization from methyl alcohol, this melted at 132.5-133.5°. It dissolved with difficulty in cold alcohol, dissolved well in ether, benzene, and chloroform. It was insoluble in both acids and bases. Upon boiling with an alkaline solution of permanganate it was slowly oxidized; it was rapidly oxidized by acid permanganate. It reacted slowly with bromine in absolute benzene, with the evolution of HBr. Its composition corresponded to that of α-(1-methyl-3-phenyl-2-indolyl)-phenylacetic acid.

Analysis for nitrogen:

3.402 mg substance: 0.92 ml 0.01 N H_2SO_4.
3.399 mg substance: 0.90 ml 0.01 N H_2SO_4.
Found %: N 3.78, 3.70.
$C_{25}H_{23}O_2N$. Computed %: N 3.79.

Analysis for C and H:

3.13 mg substance: 9.36 mg CO_2; 1.86 mg H_2O.
3.91 mg substance: 11.60 mg CO_2; 2.33 mg H_2O.
Found %: C 81.03, 80.91; H 6.65, 6.66.
$C_{25}H_{23}O_2N$. Computed %: C 81.26; H 6.28

The acid alcoholic solution of the mother liquor, after the removal of the precipitate, was concentrated in vacuum to a small volume, and made alkaline with a solution of caustic soda. The precipitate of zinc hydroxide was filtered off and carefully washed with ether. The filtrate was also extracted with ether. The united ethereal extracts were washed several times with 1:1 hydrochloric acid, then with water, and finally they were dried over anhydrous sodium sulfate. After the ether had been driven off, 0.17 g of a substance was obtained which was recrystallized from methyl alcohol and then had m.p. 129-130°. A mixed test with the material with m.p. 132.5-133.5° gave m.p. 130.5-132°. After it was made alkaline, the hydrochloric acid extract was extracted with ether. This was dried, and the ether driven off, to leave only traces of the bases.

b) 1.00 g of the methylphenylhydrazone of α,γ-diphenylacetoacetic ester was treated with an alcoholic solution of hydrogen chloride under exactly the same conditions as in experiment a), but without the addition of zinc dust. 0.81 g of a substance was obtained with m.p. 132.5-133.5°. The yield was 85% of the theoretical.

This same product was obtained by boiling the methylphenylhydrazone of α,γ-diphenylacetoacetic ester with glacial acetic acid for 0.5 hour. The acetic acid was neutralized with a 5% solution of soda. The oil which separated quickly crystallized. The precipitate was washed with water, then with cold methyl alcohol. The yield of indole derivative under these conditions amounted to 70%.

c) 0.35 g of α,γ-diphenylacetoacetic ester, 0.17 g of asymm. methylphenylhydrazine, and 3 ml of glacial acetic acid were heated on a water bath for 30 minutes. Upon cooling and rubbing with a glass stirring rod, crystallization began. Cold alcohol was added to the mixture, and the precipitate filtered with suction, washed with cold alcohol, and dried. 0.25 g of the indole derivative with m.p. 132.5-133.5° was obtained.

Before obtaining the product with m.p. 132.5-133.5°, we observed, under analogous conditions, the formation of a product with m.p. 103-104°, which crystallized with much more difficulty than the first product. After we had obtained the high-melting material in our laboratory, we were no longer able to obtain the product with m.p. 103-104°. In its chemical properties, this substance was completely identical with the indole derivative with m.p. 132.5-133.5°. Upon saponification, both these substances gave one and the same acid. In composition, the substance with m.p. 103-104°, like the high-melting product, corresponded to the ethyl ester of α-(1-methyl-3-phenyl-2-indolyl)-phenylacetic acid.

Analysis for nitrogen:

6.201 mg substance: 1.60 ml 0.01 N H_2SO_4.
6.797 mg substance: 1.70 ml 0.01 N H_2SO_4.
Found %: N 3.61, 3.51.
$C_{25}H_{23}O_2N$. Computed %: N 3.79.

0.1003 g substance: 0.2989 g CO_2; 0.0583 g H_2O.
0.1190 g substance: 0.3542 g CO_2; 0.0696 g H_2O.
Found %: C 81.28, 81.17; H 6.50, 6.49.
$C_{25}H_{23}O_2N$. Computed %: C 81.26; H 6.28.

α-(1-Methyl-3-phenyl-2-indolyl)-phenylacetic acid

0.65 g of the ethyl ester of α-(1-methyl-3-phenyl-2-indolyl)-phenylacetic acid was boiled in a solution with 2 g of KOH and 10 ml of methyl alcohol for 25 hours. The reaction mixture was diluted with water. During the dilution, the formation of cloudiness was noted. The methyl alcohol was then driven off in vacuum. The precipitated oil crystallized upon cooling. Upon the addition of water, it went into solution. In all probability, this substance was the potassium salt of the expected acid. The aqueous solution, with a volume of about 125 ml, was extracted four times with ether, and then acidified with 1:5 hydrochloric acid until there was a distinct acidity to Congo red. The precipitate which formed was allowed to stand several hours, then filtered with suction, washed with distilled water, and dried. After recrystallization from methyl alcohol, the acid melted at 142°, with a considerable evolution of gas. The substance was moderately soluble in chloroform, more soluble in ether, and soluble with difficulty in cold benzene.

Analysis for nitrogen:

3.033 mg substance: 0.98 ml 0.01 N H_2SO_4.
4.594 mg substance: 1.45 ml 0.01 N H_2SO_4.
Found %: N 4.15, 4.42.
$C_{23}H_{19}O_2N$. Computed %: N 4.10.

Analysis for C and H:

3.50 mg substance: 10.41 mg CO_2; 1.76 mg H_2O.
3.38 mg substance: 10.04 mg CO_2; 1.72 mg H_2O.
Found %: C 81.12, 81.01; H 5.61, 5.69.
$C_{23}H_{19}O_2N$. Computed %: C 80.90; H 5.61.

The thermal decarboxylation of α-(1-methyl-3-phenyl-2-indolyl)-phenylacetic acid

0.2 g of α-(1-methyl-3-phenyl-2-indolyl)-phenylacetic acid was heated on an oil bath at a temperature of 152-154° (bath temperature). The compound melted and evolved CO_2 (test with baryta water). After several minutes, the evolution of gas ceased, and heating was discontinued. Upon cooling, the reaction mixture hardened to give a solid yellow material, which, after recrystallization from alcohol, melted at 129-129.5°. This corresponded to the m.p. of the 1-methyl-2-benzyl-3-phenylindole (129-130°), previously obtained by Neber [13].

Analysis for nitrogen:

6.203 mg substance: 2.03 ml 0.01 N H_2SO_4.
9.001 mg substance: 2.99 ml 0.01 N H_2SO_4.
Found %: N 4.58, 4.64.
$C_{22}H_{19}N$. Computed %: N 4.71.

Analysis for C and H:

4.76 mg substance: 15.44 mg CO_2; 2.73 mg H_2O.
Found %: C 88.46; H 6.41.
$C_{22}H_{19}N$. Computed %: C 88.84; H 6.44.

The reduction of the methylphenylhydrazone of α,γ-diphenylacetoacetic ester with aluminum amalgam

Aluminum amalgam was prepared by the method of Wislicenus, described in Weygand's book [16].

a) 1.00 g of the methylphenylhydrazone of α,γ-diphenylacetoacetic ester was dissolved in 50 ml of moist ether, and the solution shaken with 2 g of amalgamated aluminum. From time to time a drop of water was added (a single drop after 30 minutes), and moist ether. The reduction lasted a total of 8 hours. The precipitate was filtered off and washed several times with ether. The united ether extracts were themselves extracted four times with a solution of 1:3 hydrochloric acid. When the solution was made alkaline, only traces of the base precipitated. The ether extract was dried over anhydrous sodium sulfate. The ether was driven off. 0.80 g of material was obtained, which after recrystallization from methyl alcohol melted at 90-91°, and gave no lowering of the melting point when mixed with the original material.

b) 1.00 g of the methylphenylhydrazone of α,γ-diphenylacetoacetic ester was dissolved with heating in a mixture of 25 ml of alcohol and 2 ml of water. 2 g of amalgamated aluminum was added to the solution, and the mixture was boiled on the water bath. After 11 hours, an additional 1 g of aluminum amalgam was added, plus a mixture of 10 ml of alcohol and 2 ml of water. Then after approximately equal intervals of time, three mixtures of 5 ml of alcohol and 1 ml of water were added. In all, boiling was continued for 44 hours. The precipitate was filtered off while hot, and washed with hot alcohol. The alcohol was driven off in vacuum, the residue dissolved in ether, and the ethereal solution repeatedly extracted with small portions of 1:3 hydrochloric acid. After drying over anhydrous sodium sulfate, the ether was driven off. The residue crystallized after rubbing with a glass stirring rod. 0.85 g of a material was obtained, which was recrystallized from alcohol to have a m.p. of 90-91°. This gave no lowering of the melting point when mixed with the original substance. The acid extract was made alkaline with a solution of NaOH, extracted with ether, and the ether extract dried over anhydrous sodium sulfate. The ether was driven off to leave only 0.03 g of a substance of an oily nature.

SUMMARY

1. It has been shown that the reaction between phenylhydrazine and α,γ-diphenylacetoacetic ester gives 1,4-diphenyl-3-benzyl-5-pyrazolone even at room temperature.

2. The reaction between asymm. methylphenylhydrazine and α,γ-diphenylacetoacetic ester takes place only upon heating on the boiling water bath for several hours, and leads to the formation of the normal product – the methylphenylhydrazone of α,γ-diphenylacetoacetic ester.

3. It has been shown that, in contrast to the results of Volhard, the heating of α,γ-diphenylacetoacetic ester with hydrazine hydrate in alcoholic solution on the water bath for an hour leads to the immediate formation of 4-phenyl-3-benzyl-5-pyrazolone. The substance with m.p. 125-126°, accepted by Volhard as the hydrazone of α,γ-diphenylacetoacetic ester, is an impure form of this pyrazolone.

4. The reduction of the methylphenylhydrazone of α,γ-diphenylacetoacetic ester by the method of Feofilaktov (with zinc and alcoholic hydrogen chloride) has been investigated. It has been found that under these conditions, the compound is not reduced, but rearranges to give an indole derivative.

The attempt to reduce the methylphenylhydrazone of α,γ-diphenylacetoacetic ester with aluminum amalgam gave an almost complete recovery of the compound from the reaction in unaltered form.

The methylphenylhydrazone of acetoacetic ester is apparently reduced normally by Feofilaktov's method.

5. The rearrangement of the methylphenylhydrazone of α,γ-diphenylacetoacetic ester to give an indole derivative has been investigated. It has been found that it takes place with ease when this hydrazone is treated in alcoholic solution with hydrogen chloride, even during cooling with ice water. It has been shown that this indole derivative is the ethyl ester of α-(1-methyl-3-phenyl-2-indolyl)-phenylacetic acid.

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AN INVESTIGATION OF THE SUBSTITUTION OF THE HALOGEN IN α-HALOGEN CARBONYL COMPOUNDS*

III. THE REACTIONS OF α CHLOROBENZYLMETHYLKETONE AND α-CHLORO-(p-TOLYL)-ACETONE WITH SALTS OF CARBOXYLIC ACIDS

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T.I.Temnikova has shown previously that in the reaction of α-bromobenzylmethylketone with the potassium salts of acetic and benzoic acids, the substitution of the halogen takes place in an anomalous manner. As a result, there are formed, in addition to the esters of phenylacetylcarbinol, which correspond to the structure of the original bromoketone, the isomeric esters of methylbenzoylcarbinol [1]. With potassium acetate, α-bromo-(p-tolyl)-acetone also forms a mixture of the acetates of p-tolylacetylcarbinol and of p-toluylmethylcarbinol, the normal product of the reaction predominating [2].

In order to carry on the investigation of the substitution of the halogen in α-halogen ketones, we investigated, in the present work, the α-chloroketones corresponding to the indicated α-bromoketones: α-chlorobenzylmethylketone, $C_6H_5CHClCOCH_3$, and α-chloro-(p-tolyl)-acetone, p-$CH_3C_6H_4CHClCOCH_3$. This investigation was expected to give an answer to the question as to whether the course of the reaction, i.e., the yields of isomeric esters, was determined by the nature of the halogen in the molecule of α-halogen ketone.

α-Chlorobenzylmethylketone was obtained by the chlorination of the ketone with elementary chlorine in chloroform solution. Of its various properties, its ease of oxidation by the air attracted atention. This is also characteristic of other chloroketones, as for example, of the α-chloro-(p-tolyl)-acetone described below, and also of α-chlorocyclooctanone.

The reaction with potassium benzoate was carried out by the method described [1]. The reaction gave a mixture of benzoates which were easily separated as a result of the different solubilities of the isomers in absolute ether. From 15 g of the chloroketone, 8 g of the ester with normal structure was obtained, and 1 g of the isomeric ester. The content of isomeric ester amounted, therefore, to about 10% of the products of the reaction, or to 4% based on the original chloroketone. As has been shown [1], 5 g of the bromoketone give 0.1 g of the isomeric benzoate, which amounts to about 2%, based on the original bromoketone.

Thus, in both cases, the yield of anomalous benzoate amounts to about the same order of magnitude.

Similar results were also obtained in the investigation of the reaction of α-chloro-(p-tolyl)-acetone with potassium acetate.

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*The present investigation is the continuation of the previous series of articles in this field carried on in collaboration with T. I. Temnikova and printed in the J. Gen. Chem. 11,1 (1941), and 19, 1318 (1949) for which last see CB translation p. 1315 ff.

The chloroketone was obtained by the action of sulfuryl chloride on the ketone in carbon tetrachloride solution.

The reaction with potassium acetate was completed in 1.5 hours, and gave a liquid product, whose composition corresponded to that of the acetate, with b.p. 136-139° at 5 mm. The properties of this compound were similar to those of the products obtained from the bromoketone. In addition, there formed during the reaction a small amount of p-toluic acid, apparently as the result of oxidation of the chloroketone.

The proof of the structure of the acetate with b.p. 136-139° at 5 mm was carried out in exactly the same way as in the investigation of the bromoketone [2]. By the action of methylmagnesium bromide, the ester was converted into a glycol, and the latter was oxidized with lead tetracetate.

The oxidation of 1.7 g of glycol gave 0.13 g of the semicarbazone of p-tolylmethylketone, and in addition, acetone and p-toluic aldehyde. It had been shown previously that in the analogous investigation of the bromoketone, 2.5 g of the glycol obtained from the acetate gave, upon oxidation, 0.19 g of the semicarbazone of p-tolylmethylketone.

Therefore, here too, as in the case of the bromoketone, the glycol is a mixture of 1-(p-tolyl)-2-methylpropanediol-1,2 and 1,1-(p-tolyl)-methylpropanediol-1,2. This shows that the product with b.p. 136-139° at 5 mm is a mixture of the acetates of p-tolylacetylcarbinol and of p-toluylmethylcarbinol, with a considerable predominance of the former.

In both cases, both with the bromoketone and with the chloroketone, judging by the oxidation products of the glycols, the mixture of these acetates obtained was in approximately the same ratio.

The present investigation shows that if bromoketones are capable of giving anomalous substitution products in the reaction with salts of carboxylic acids, then the corresponding chloroketones react in the same way, and form reaction products in approximately the same ratios.

Thus, in the halogen ketones under investigation, with the general formula $ArCHHalCOCH_3$, the nature of the halogen does not play a determining role in the mechanism of the substitution of the halogen by the ester group. The structure of the molecule of the halogen ketone is of incomparably greater significance. Although the chloroketones react much more slowly than the bromoketones, this fact had no essential influence on the mechanism of the substitution.

EXPERIMENTAL

1. The Preparation of α-Chlorobenzylmethylketone

The ketone in $CHCl_3$ solution was treated with an equivalent amount of chlorine while the solution was cooled and stirred. The product of chlorination was repeatedly fractionated in vacuum with the use of a column. The chloroketone with b.p. 99-101° at 4 mm was finally obtained in 20% yield.

0.2085 g substance: 0.1763 g AgCl (Carius).
0.2792 g substance: 0.2355 g AgCl.
Found %: Cl 20.90, 20.90.
C_9H_9OCl. Computed %: Cl 21.03.

$d_4^{17.7}$ 1.160; d_4^{0} 1.177; d_4^{20} 1.1585; $n_\alpha^{17.7}$ 1.5339; $n_\beta^{17.7}$ 1.5504.

Found: MR_α 44.9; MR_β 46.05; $MR_{\beta-\alpha}$ 1.15.
$C_8H_9OCl\Gamma_3$. Computed: MR_α 44.73; MR_β 45.74; $MR_{\beta-\alpha}$ 1.00.

Richard [4] obtained chlorobenzylmethylketone by the action of sulfuryl chloride on the ketone.

B.p. 122.5-123° at 15 mm; n_D^{20} 1.53567; d_4^{20} 1.1574.

Upon long standing in a loosely stoppered flask, the chloroketone was completely oxidized, with the formation of benzoic acid.

The Action of Potassium Benzoate on the Chloroketone

15 g of the chloroketone (b.p. 99-101° at 4 mm) was heated on the water bath with 20 g of potassium benzoate in 120 ml of absolute alcohol for 10 hours. However, as this solution continued to show a positive reaction for halogen, the heating was continued up to 50 hours. In this way, the reaction was carried to a conclusion. By means of the usual treatment [1], we obtained 8.5 g of a substance with m.p. 52-53°, soluble in absolute ether, and 1 g with m.p. 107.5-108°, insoluble in absolute ether. The identity of these compounds with the benzoates of phenylacetylcarbinol and methylbenzoylcarbinol respectively was confirmed by mixed tests.

2. The preparation of α-Chloro-(p-tolyl)-acetone

The chloroketone was obtained by treating the ketone with sulfuryl chloride in a solution of CCl_4 at 30°. Toward the end, the temperature was raised to 50°.

From 23 g of ketone (b.p. 111-114° at 11 mm), 12 g of the chloroketone with b.p. 118-120° at 5 mm were obtained.

0.2195 g substance: 0.1721 g AgCl (Stepanov).
0.1743 g substance: 0.1382 g AgCl.
Found %: Cl 19.40, 19.60.
$C_{10}H_{11}OCl$. Computed %: Cl 19.41.

d_4^{20} 1.129; d_4^{16} 1.132; n_α^{16} 1.5302; MR_α 49.86.

$C_{10}H_{11}OCl\Gamma_3$. Computed: MR_α 49.32.

The chloroketone had a comparatively weak lachrymatory action. Upon standing in the air it oxidized to give p-toluic acid.

The Action of Potassium Acetate on the Chloroketone

To a warm solution of 10.5 g of potassium acetate in 60 ml of absolute alcohol, there was added 10.5 g of the chloroketone. The reaction began at once. After 1.5 hours of heating on the water bath, a test for halogen in the solution gave a negative result.

After the usual treatment [2], 5.6 g of the acetate with b.p. 136-139° at 5 mm was obtained.

n_α^{20} 1.5053; d_4^0 1.097; d_4^{20} 1.080.
Found: MR_α 56.67.
Computed: MR_α 55.20.

0.1572 g substance: 0.4004 g CO_2; 0.1000 g H_2O.
Found %: C 69.50; H 7.10.
$C_{12}H_{14}O_3$. Computed %: C 69.88; H 6.84.

In addition, among the products of the reaction, p-toluic acid (0.3 g) was detected in the water layer. This, obviously, had formed as a result of the oxidation of the chloroketone during the reaction.

By the method described [2], 4 g of the acetate gave 2 g of glycol with b.p. 140-141° at 4 mm.

0.1292 g substance: 0.3458 g CO_2; 0.1096 g H_2O.
Found %: C 73.00; H 9.50.
$C_{11}H_{16}O_2$. Computed %: C 73.30; H 8.95.

1.7 g of glycol was oxidized with 4.7 g of lead tetracetate. The easily volatile substances were driven off, by heating the reaction mixture to 75°, into a solution of ammoniacal silver oxide, which had been prepared according to directions [5]. A faint black cloudiness was formed, possibly because of traces of acetaldehyde. After the solution had been neutralized, the first 25 ml of distillate was collected in a solution of p-nitrophenylhydrazine. We obtained 0.17 g of the p-nitrophenylhydrazone of acetone (m.p. 143-144.5°).

After the easily volatile substances had been driven off, the remaining products of oxidation were also distilled with steam into a solution of ammoniacal silver oxide (from 4 g of $AgNO_3$). A good silver mirror was thus formed. The solution was neutralized with sulfuric acid, and the neutral products were distilled off with steam. To the emulsion which was obtained, an oxidizing mixture prepared from 1.2 g of $AgNO_3$ was added. However, after standing for a day, no silver mirror had formed.

After the mixture had been acidified, the neutral products were again distilled off, and extracted with absolute ether. The ether was driven off, and the yellow oil which remained was treated with a solution of semicarbazide. 0.13 g of semicarbazone was obtained. This, after two recrystallizations from methyl alcohol, had m.p. 192-194.5°, and appeared to be completely identical with the sample of semicarbazone of p-tolylmethylketone described in the investigation of α-bromo-p-tolylacetone [2].

The acid obtained by oxidizing the neutral products with silver oxide was distilled off with steam. It had m.p. 178-179°, and was identical with p-toluic acid.

The author takes the occasion to express his profound thanks to Prof. T.I. Temnikova for her valuable direction and cooperation in this work.

SUMMARY

It has been shown that the α-bromo- and α-chloro ketones of the general formula $ArCHHalCOCH_3$ react with salts of carboxylic acids to give approximately the same ratios of products of normal and of anomalous substitution, independent of the nature of the halogen in the molecule of the original halogen ketone.

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AN INVESTIGATION OF THE SUBSTITUTION OF THE HALOGEN IN α-HALOGEN CARBONYL COMPOUNDS

IV. THE MECHANISM OF THE SUBSTITUTION OF THE HALOGEN IN α-BROMO AND α-CHLORO KETONES IN THE REACTION WITH SALTS OF CARBOXYLIC ACIDS

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In 1936, T.I.Temnikova for the first time showed, by the example of α-bromobenzylmethylketone, that the reaction between halogen ketones and salts of carboxylic acids took an anomalous course. The ketones reacted with potassium acetate to give chiefly the isomeric ester, a product of anomalous substitution, along with a small amount of the ester with normal structure. With potassium benzoate, however, the isomeric ester was obtained in small amount, and the chief product was the normal ester.

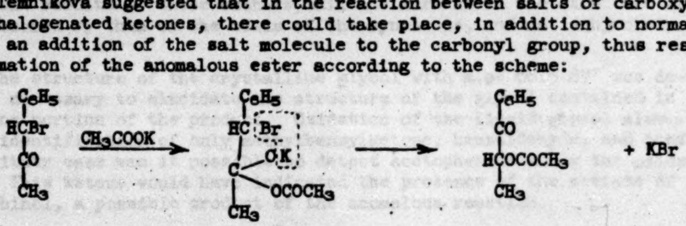
α-Bromopropiophenone, however, reacted normally with both salts [1].

It was further shown that, in contrast to the previously investigated α-bromobenzylmethylketone, α-bromo-p-tolylacetone, which had a methyl group in the para position in the phenyl nucleus, also reacted with potassium acetate to give a mixture of the normal and the isomeric acetates, the normal ester, however, considerably predominating [2].

In 1938, Blatt confirmed the results of T.I.Temnikova with α-bromodiketones of the general formula ArCOCOCHBrAr, which formed the isomeric acetates $ArCOCH(OCOCH_3)COAr$ with potassium acetate. The α-dibromodiketones ArCOCHBrCOAr give only the esters of normal structure [3].

In 1944, Hibbert and his coworkers showed that the reaction of 1-(3,4-dimethoxyphenyl)-3-chloropropanone-2 – $(CH_3O)_2C_6H_3CH_2COCH_2Cl$ – with potassium acetate gave the isomeric ester $(CH_3O)_2C_6H_3COCH(OCOCH_3)\ CH_3$ [4].

T.I.Temnikova suggested that in the reaction between salts of carboxylic acids and halogenated ketones, there could take place, in addition to normal substitution, an addition of the salt molecule to the carbonyl group, thus resulting in the formation of the anomalous ester according to the scheme:



The yields of normal and of the isomeric esters would depend on the ratio of the reaction velocity of the formation of the intermediate addition product and the velocity of direct substitution. The formation of an intermediate compound between the halogen ketone and the salt would be determined by the tendency of the carbonyl group to form addition compounds.

In order to test this suggested mechanism, and to carry our investigation of the mechanism of anomalous substitution further, we investigated α-bromohexylmethylketone $CH_3(CH_2)_4CHBrCOCH_3$, which contains a carbnnyl group in its molecule in the form of the acetyl grouping, in the same way as α-bromobenzylmethylketone. However, it became evident that this bromoketone reacted only in the normal way [5] with potassium acetate and potassium benzoate. Therefore, the presence of the acetyl group was not enough to determine the tendency of α-halogenated ketones to take part in anomalous substitution reactions. It was necessary to assume that the character of the radicals in the molecule of the bromoketone also played a part.

In order to clarify the situation, we undertook the investigation of α-bromodibenzylketone, $C_6H_5CHBrCOCH_2C_6H_5$, which contains a phenyl radical in the α-position to the carbonyl, just as in the case of α-bromobenzylmethylketone, but does not contain the acetyl grouping CH_3CO.

The α-bromoketone (m.p. 48-48.5°) was obtained in accordance with the data in the literature [7]. The reaction with potassium acetate in a solution of absolute alcohol was completed in 15 minutes. In a solution of glacial acetic acid, the reaction required heating for 3 hours. The product of the reaction, the acetate, partially decomposed and formed a tar upon distillation (b.p. 195-195.5° at 6 mm). Therefore, the investigation was carried out both on the distilled and on the crude product, in the case where the latter had a composition close to that theoretically required.

In order to show its structure, the acetate was treated with an excess of CH_3MgBr. This gave a crystalline glycol with m.p. 86.5-87°. In addition to the crystalline glycol, a portion of the product was obtained in liquid form.

The glycol was characterized by its ability to form a compound containing benzene of crystallization, with the formula $C_{16}H_{18}O_2 \cdot C_6H_6$. Similar compounds with benzene are known for diphenylglycolic aldehyde [8] and mandelic acid [9].

The crystalline glycol was oxidized with chromic anhydride in a solution of acetic acid, and among the products of oxidation there were found benzaldehyde and benzylmethylketone. Therefore the glycol with m.p. 86.5-87° was 1,3-diphenyl-2-methylpropanediol-1,2, $C_6H_5CHOHCOH(CH_3)CH_2C_6H_5$, and could have been obtained only from the acetate of normal structure, $C_6H_5CH(OCOCH_3)COCH_2C_6H_5$.

For the α-form of 1,3-diphenyl-2-methylpropanediol-1,2 Tiffenault, Levy, and Weyl give m.p. 96-97°; the stereoisomeric β-form is liquid [10]. We are therefore forced to doubt the results of these authors, all the more so as the structure of the glycol was assumed by them on the basis of the synthesis, and not subjected to direct proof.

Although the structure of the crystalline glycol with m.p. 86.5-87° was determined, it was necessary to elucidate the structure of the glycol contained in the noncrystalline portion of the product. Oxidation of the liquid glycol also resulted in the identification of only methylbenzylketone, benzaldehyde, and benzoic acid. In neither case was it possible to detect acetophenone among the oxidation products. This ketone would have indicated the presence of the acetate of benzylbenzoylcarbinol, a possible product of the anomalous reaction.

Thus, it has been shown that the action of potassium acetate on α-bromodibenzylketone results in only normal substitution.

In addition, the action of potassium benzoate on the bromoketone was investigated. A crystalline benzoate with m.p. 82.5-83.5° appeared to be the sole product of the reaction. It was impossible to detect in this any admixture of an isomeric ester.

For purposes of comparison, we synthesized the isomeric benzoate of benzylbenzoylcarbinol from α-bromobenzylacetophenone and potassium benzoate. The results listed below indicate that halogenated ketones with a benzoyl grouping react with salts of carboxylic acids to give normal substitution products. Basing our conclusions on these results, we expected the benzoate to have the following structure: $C_6H_5COCH(OCOC_6H_5)CH_2C_6H_5$.

The benzoate we synthesized had m.p. 109-110°, and in no way resembled the benzoate with m.p. 82.5-83.5°, which we had obtained from α-bromodibenzylketone. This very fact confirmed the structure of the latter as an ester of phenylacetyl phenylcarbinol, i.e., as a product of the normal reaction, $C_6H_5CH(OCOC_6H_5)COCH_2C_6H_5$.

It was thus shown that α-bromodibenzylketone reacts with potassium acetate and potassium benzoate in only the normal manner. The substitution of the halogen by an ester residue gives esters corresponding to the structure of the original bromoketone.

By comparing this fact with the other results in our possession, we can indicate the mechanism of the reaction under investigation.

A summary of the verified results on the reaction between salts of carboxylic acids and α-halogen ketones of different structure is given in Table 1.

TABLE 1

Experimental results on the course of the reaction between salts of carboxylic acids and α-halogen ketones

General formula	Isomeric esters obtained	No isomeric esters obtained
RCHHalCOCH$_3$	1) α-Chloro(bromo)-benzylmethylketone, $C_5H_5CHCl(Br)COCH_3$ [1,11] 2) α-Chloro(bromo)-p-tolylacetone, $p\text{-}CH_3C_6H_4CHCl(Br)COCH_3$ [2,11]	1) α-chloro(bromo)-acetone, $CH_3COCH_2Cl(Br)$ [39] 2) α-Bromohexylmethylketone, $CH_3(CH_2)_4CHBrCOCH_3$ [5]
RCHHalCOR'		1) α-Bromopropiophenone, $C_6H_5COCHBrCH_3$ [1] 2) 1-(3,4-Dihydroxyphenyl)-2-bromopropanone-1, $(CH_3O)_2C_6H_3COCHBrCH_3$ [4] 3) α-Bromobenzylacetophenone, $C_6H_5COCHBrCH_2C_6H_5$ 4) α-Bromo-(p-chloro)-propiophenone, $p\text{-}ClC_6H_4COCHBrCH_3$ [20] 5) α-Bromodibenzylketone, $C_6H_5CHBrCOCH_2C_6H_5$
RCOCH$_2$Hal	1-(3,4-Dimethoxyphenyl)-3-chloropropane-2 $(CH_3O)_2C_6H_3CH_2COCH_2Cl$ [4]	
RCHHalCOCOR'	$C_6H_5CHBrCOCOC_6H_5$ [3] $C_6H_5CHBrCOCOC_6H_4OCH_3$ [3] $CH_3OC_6H_4CHBrCOCOC_6H_5$ [3]	
RCOCHHalCOR'		$C_6H_5COCHBrCOC_6H_5$ [3] $CH_3OC_6H_4COCHBrCOC_6H_5$ [3]

It is evident from Table 1 that the course of the reaction we are investigating is determined by structural factors and the structure of the α-halogen ketone molecule. The nature of the radical next to the carbonyl group plays a decisive role. It is chiefly halogen ketones with the acetyl grouping CH_3CO which tend to give the anomalous reaction. On the other hand, halogen ketones with the benzoyl grouping C_6H_5CO do not tend to give the anomalous reaction. However, this condition alone is not sufficient, as can be seen from the example of α-bromohexylmethylketone, $CH_3(CH_2)_4CHBrCOCH_3$, which reacts with salts of carboxylic acids normally. For the reaction to take place anomalously, there must necessarily be present, along with the acetyl grouping, an aromatic radical in the β-position to the carbonyl. The nature of the halogen in the molecule of α-halogen ketone exerts no essential influence on the course of the reaction [11].

The role of the structural factors may be related to the ability of the carbonyl group in ketones of different structures to react. Petrenko-Kritchenko has shown [8] that ketones containing the acetyl grouping, CH_3CO, in the presence of unbranched radicals, have the greatest ability to react with such reagents as phenylhydrazine and hydroxylamine. Ketones which do not have the acetyl grouping have a considerably lower ability to react.

On the other hand, if there is a benzoyl grouping, C_6H_5CO, in the ketone, then the ketone has very little ability to react with these reagents (Table 2). It is also known that the α-diketones containing both a benzoyl and an acetyl grouping, acetylbenzoyl, $C_6H_5COCOCH_3$, reacts with semicarbazone primarily because of the acetyl carbonyl [12].

TABLE 2

Ability of different ketones to react

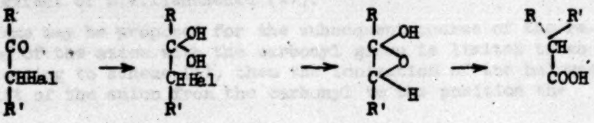
Ketone		Reaction velocity (%) per hour	
		with phenylhydrazine	with hydroxylamine
Acetone	CH_3COCH_3	51	82
Methylethylketone	$CH_3COC_2H_5$	38.1	79
Methylpropylketone	$CH_3COC_3H_7$	27	74
Methylhexylketone	$CH_3COC_6H_{13}$	25.7	67
Methylbenzylketone	$CH_3COCH_2C_6H_5$	24.1	—
Methylisopropylketone	$CH_3COCH(CH_3)_2$	15.6	33
Pinacoline	$CH_3COC(CH_3)_3$	3.6	—
Diethylketone	$C_2H_5COC_2H_5$	12.4	38
Dipropylketone	$C_3H_7COC_3H_7$	7.1	31
Acetophenone	$CH_3COC_6H_5$	4.1	9.2
Propiophenone	$C_2H_5COC_6H_5$	1.7	—

From a comparison of the data of Tables 2 and 1, it is evident that it is precisely those halogen ketones which contain a relatively more active acetyl group, CH_3CO, which tend toward the anomalous reactions with the salts of carboxylic acids, and that it is those which have the inactive benzoyl group, C_6H_5CO, which lack this tendency.

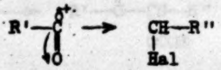
There therefore arises the question of the role of the carbonyl group in general during the substitution of the halogen in α-halogenated ketones. It is known that in α-halogenated ketones the halogen has a greatly increased mobility and is substituted with extraordinary ease. However, if the carbonyl group is not free, the situation is altered. Thus, Evlampiev showed that the diethyl ketals of α-chloro (or bromo- or iodo)-acetone, $CH_3C(OC_2H_5)_2CH_2Cl$ (Br, I), were completely incapable of exchanging their halogen under the action of the most powerful alkaline reagents [16].

Therefore, the increased mobility of the halogen in α-halogenated ketones is related to the presence of a free carbonyl group. It is precisely the presence of the latter which makes it extraordinarily easy to substitute the halogen, and determines the mechanism of the reaction.

A sketch of the mechanism of substitution of the halogen in α-halogenated ketones in the reaction with salts of carboxylic acids can be given on the basis of the scheme of A.E.Favorsky, proposed by him as far back as 1894 as an explanation of the action of alkali on halogenated ketones, and on the basis of the analogous scheme by T.I.Temnikova, given above. In accordance with the ideas of A.E. Favorsky, it is as a result of the influence of the neighboring halogen that the carbonyl group has an increased ability to form addition compounds. The first step of the reaction is the addition to the carbonyl of the reagent (like water or HCN). Then, under the influence of the medium (alkali), hydrogen halide splits off, and there is a rearrangement [14]:



The structure of the halogenated ketone may be written in the following manner:

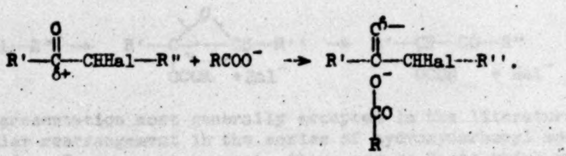


$$R'-\overset{\delta+}{C}(\curvearrowleft\!=\!O)-CH(Hal)-R''$$

Because of the influence of the halogen, the (+) charge on the carbon atom is increased. This also explains the increased tendency of the carbonyl group to form addition compounds.

In 1941, Beker showed that ω-halogenacetophenones which were substituted in the nucleus reacted with pyridine more quickly the greater the influence the substituents in the nucleus had on -I and -M, i.e., the greater the (+) charge on the carbon atom of the carbonyl, and thus confirmed the scheme of A.E.Favorsky [15].

In accordance with A.E.Favorsky's scheme, the first step of the reaction between the halogenated ketone and the salt may be written in the following manner:

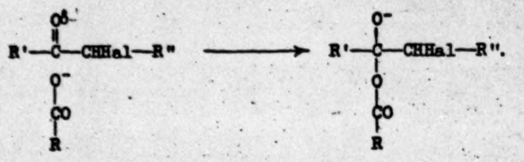


$$R'-\underset{\delta+}{\overset{O}{\overset{\|}{C}}}-CHHal-R'' + RCOO^- \dashrightarrow R'-\underset{O^- - CO - R}{\overset{O^{\delta-}-}{\overset{\|}{C}}}-CHHal-R''. \qquad (1)$$

There first takes place an ion-dipole interaction between the anion and the carbon atom of the carbonyl, whose intensity is determined by the magnitude of the (+) charge on the carbon atom and the nucleophilic tendency of the anion.

As a result of this interaction, the (+) charge on the carbonyl carbon is neutralized, and the (-) charge on the oxygen atom is increased.

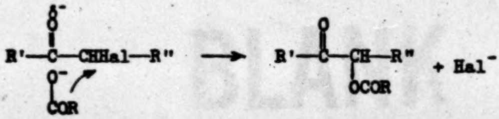
As a limiting case, we might have the formation of a covalent bond between the anion and the carbonyl carbon, with the formation of a univalent negative oxygen atom:


(2)

As a result of the increase of the (-) charge on the oxygen of the carbnnyl, the ionization of the halogen is made easier. This also explains its mobility in halogenated ketones during substitution reactions.

In ketals, investigated by Evlampiev, a similar polarization of the carbonyl (increase of the (-) charge on the oxygen) is impossible. Therefore, the ionization of the halogen is not stimulated, but on the other hand, is made more difficult, as the result of the presence of the ketal group. This is in accordance with the theory of the vicinal effect of D.V.Tishchenko [17].

Two possible mechanisms may be proposed for the subsequent course of the reaction. If the interaction of the anion with the carbonyl group is limited to an ion-dipole interaction according to scheme (1), then the ionization of the halogen will be completed by a shift of the anion from the carbonyl to the position the halogen occupied:

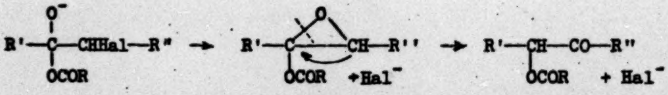

(3)

Thus an ester is obtained whose structure corresponds to that of the original halogenated ketone, i.e., to the product of normal substitution.

However, if the reaction of the anion with the carbonyl group leads to the formation of a covalent bond in accordance with scheme (2), then it is possible that not the anion, but the oxygen will make the shift.

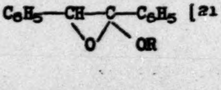
This shift may be pictured as taking place either by means of the formation of an intermediate alcohol oxide ether, or by intramolecular rearrangement which passes through the stage of the formation of an oxygen ring.

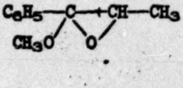
The first variant is described by scheme (4a):


(4a)

and corresponds to the presentation most generally accepted in the literature to explain the intramolecular rearrangement in the series of hydroxycarbonyl and halogen carbonyl compounds. However, at present there are no facts which would confirm or refute this scheme.

However, there are data, although they are not numerous, which indicate that alcohol oxide derivatives may exist as independent end products, despite the fact that they are occasionally unstable. Such would be the ethers of the alcohol oxides:

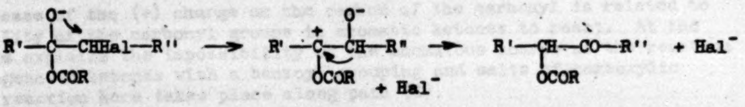

[21] and


[29]

and possibly the oxoctenol of Butlerov, and its homologs [18]. We shall assume that the alcohol oxide compounds are not necessary intermediate products in the reaction under investigation.

We prefer to accept the second variant, of direct intramolecular rearrangement of the carbonyl oxygen, analogous to that assumed by A.E.Favorsky in his explanation of the isomerization of ketones. This supposes that in the various cases there is a direct exchange of position between the carbonyl oxygen and the radicals, without the momentary formation of an oxide [22].

This step may be pictured in the following manner:

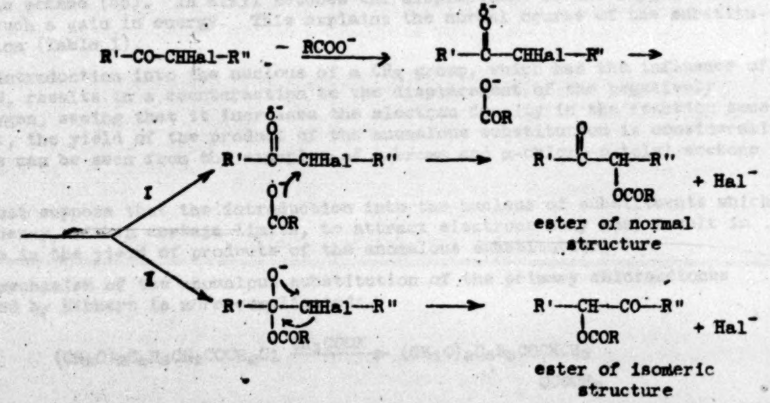


(4b)

The univalent negatively charged oxygen is shifted to the neighboring carbon with its electron pair, and because of its attempt to form a covalent bond, so to speak expels the hydrogen atom, which undergoes displacement in the same manner as with pinacoline.

Reaction (4b) gives an ester of isomeric structure.

The overall scheme for the mechanism of the reaction for the substitution of the halogen by the ester residue may be presented in the following form:



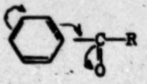
(5)

The relative velocity of the reaction along paths I and II determines the yields of esters of normal and isomeric structure, or in other words, the products of normal and anomalous substitution.

This scheme enables us to explain the experimental results obtained (Table 1).

Those halogenated ketones which have an active carbonyl group with a large (+) charge on the carbon atom have the greatest tendency toward the anomalous substitution reaction, as only in this case can a stable covalent bond be formed in accordance with scheme (2). Halogenated ketones with the acetyl grouping, CH_3CO, are the ones which satisfy this requirement to the greatest degree.

In aromatic and alkylaromatic ketones which contain a benzoyl grouping, the interaction of the phenyl nucleus and the carbonyl may be pictured in a structure which is characterized by a low value of the (+) charge on the carbon of the carbonyl:



The presence of such a structure is shown by the increased value of the dipole moment of the carbonyl group in alkyl aromatic ketones in comparison with the value in alkyl ketones: 2.94 D in acetophenone, and 2.99 D in benzophenone, compared to 2.6 to 2.7 D for alkyl ketones [13].

The decrease of the (+) charge on the carbon of the carbonyl is related to the slight ability of the carbonyl groups in aromatic ketones to react. At the same time, this explains the impossibility of the anomalous course of the reaction between α-halogenated ketones with a benzoyl grouping and salts of carboxylic acids, as the reaction here takes place along path (I).

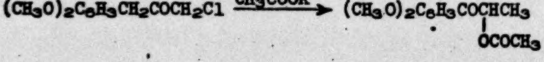
Further, as has been shown above, in addition to an active carbonyl group, the presence of a phenyl group in the molecule is needed for the reaction to take an anomalous course.

The presence of a phenyl group in the β-position to the carbonyl favors the displacement of the carbonyl oxygen, as the rearrangement results in the formation of a stable conjugated C_6H_5CO group. In addition, the hydrogen atoms on the carbon attached to the nucleus are especially mobile, and this favors displacement according to scheme (4b). In alkyl ketones the displacement of the oxygen cannot result in such a gain in energy. This explains the normal course of the substitution reaction (Table 1).

The introduction into the nucleus of a CH_3 group, which has the influence of a +I and +M, results in a counteraction to the displacement of the negatively charged oxygen, seeing that it increases the electron density in the reaction zone. As a result, the yield of the product of the anomalous substitution is considerably lowered, as can be seen from the examples of α-bromo and α-chloro-p-tolyl acetone [2,11].

We must suppose that the introduction into the nucleus of substituents which have a tendency, within certain limits, to attract electrons away must result in an increase in the yield of products of the anomalous substitution.

The mechanism of the anomalous substitution of the primary chloroketones investigated by Hibbert is more complicated:



$$(CH_3O)_2C_6H_3CH_2COCH_2Cl \xrightarrow{CH_3COOK} (CH_3O)_2C_6H_3CO\underset{\displaystyle OCOCH_3}{\underset{|}{C}H}CH_3$$

Here there is the additional phenomenon of the migration of the hydrogen to the β-position, analogous to what is observed in the rearrangement of hydroxyaldehydes (E.D.Venus-Danilova and V.F.Kazimirova [23,24]), in the acid transformations of α-chloroketones (McFee and Klingsberger [25]), and in the saponification of chloromethylethylketone in the presence of oxides of heavy metals (S.N.Danilov and N.Tikhomirova [26]).

$$RCH_2CHOHCHO \longrightarrow RCHOHCOCH_3$$

$$C_6H_5CHClCOCH_3 \longrightarrow C_6H_5CH_2CH_2COOH$$

$$C_2H_5COCH_2Cl \longrightarrow CH_3CHOHCOCH_3$$

The mechanisms submitted by the authors to explain these transformations are based on the assumption of a series of enolizations one after the other, the final result being a shift of the hydrogen atoms.

The substitution of the halogen in α-halogenated ketones which interact with salts of carboxylic acids deserves a definite place among the number of other reactions involving the substitution of halogen in these compounds.

The most important and the most thoroughly investigated is the reaction between halogenated ketones and aqueous and alcoholic alkalies or alcoholates. By means of these reactions there are formed: 1) acids (or their esters); 2) keto-alcohols (or their ketals or ethers); and in certain cases, 3) ethers of alcohol oxides.

As E.D.Venus-Danilova has shown, the yield of acid with a given halogenated ketone depends on the strength of the alkali used. The stronger the alkali, the greater the yield of acid [27].

The greatest interest lies in the data to be found in the literature on the interaction of halogenated ketones with alcoholic alkalies and alcoholates, as in these cases the transformations take many different forms, and their course is determined by the structure of the molecule of the original halogenated ketone.

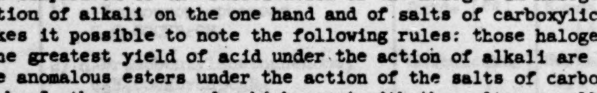
A comparison of the data to be found for primary and secondary halogenated ketones (Table 3) leads to the conclusion that the halogenated ketones which contain an acetyl grouping, CH_3CO, give, in these cases, the greatest yield of acid. On the other hand, halogenated ketones with a benzoyl grouping are incapable of being transformed into acids. The presence of a phenyl group in the β-position to the carbonyl in the molecule of halogenated ketone favors the transformation into acid.

Thus, a comparison of the substitution of the halogen in halogenated ketones under the action of alkali on the one hand and of salts of carboxylic acids on the other makes it possible to note the following rules: those halogenated ketones which give the greatest yield of acid under the action of alkali are also capable of giving the anomalous esters under the action of the salts of carboxylic acids. On the other hand, those compounds which react with the salts normally, under the action of alkali give not acids, but chiefly carbonyl compounds (or oxides).

These rules may be explained by the fact that both types of reaction take place according to a general mechanism which has the steps described in shcemes (1) and (2).

If the carbonyl group has a weak tendency to form addition compounds, then the ion-dipole interaction of the anion (hydroxyl, alkoxyl, or ester residue) with the carbonyl takes place according to scheme (3): the anion takes the position vacated by the halogen, and substitution proceeds normally. On the other hand, in case there is a powerful interaction of the anion and the carbonyl (scheme 2), a new bond is formed, and the possibility of rearrangement arises.

However, the course of the rearrangement itself is determined by the nature of the anion X. If X = RCOO, the transformation takes place according to shceme (4b), with a shift of the carbonyl oxygen. If, however, X = OH, or OR, the carbonyl is stabilized in the form of a carboxyl group, and a shift of the radical takes place:



$$R'-\overset{O^-}{\underset{X}{C}}-CHHal-R'' \longrightarrow (R''R')CHC\overset{O}{\underset{X}{\lessdot}} + Hal^-. \qquad (6)$$

X = OH, OR.

TABLE 3

Experimental results on the products of the substitution of the halogen in α-halogenated ketones under the action of various reagents

General formula of halogenated ketone	Halogenated ketone investigated	End products of reaction	
		Under action of alcoholic alkalies (alcoholates)	Under action of salts of carboxylic acids
$RCHHalCOCH_3$	1) α-Chloro(bromo)-acetone, $CH_3COCH_2Cl(Br)$	Ketal [32]	Normal ester [33]
	2) α-Chloroethylmethylketone, $CH_3COCHClCH_3$	Alkoxyketone [28]	-
	3) α-Bromohexylmethylketone, $CH_3COCHBr(CH_2)_4CH_3$	-	Normal ester [5]
	4) α-Chloro(bromo)-benzylmethylketone, $CH_3COCHBr(Cl)C_6H_5$	Acid 60%, alkoxyketone or ketal 20-30%, [25,29]	Isomeric esters [1,11]
	5) α-Chloro(bromo)-p-tolylacetone, $CH_3COCHBr(Cl)C_6H_4CH_3$	-	Isomeric esters [2,11]
$RCOCH_2Hal$	1-(3,4-Dimethoxy)-phenyl-3-chloropropanone-2, $(CH_3O)_2C_6H_3CH_2COCH_2Cl$	Acid [25]	Isomeric ester, [4]
$C_6H_5COCHHalR$	1) α-Bromopropiophenone, $C_6H_5COCHBrCH_3$	Oxide [29]	Normal ester [1]
	2) α-Bromobenzylacetophenone, $C_6H_5COCHBrCH_2C_6H_5$	Ketoalcohol° [31]	Normal benzoyl ester
$RCHHalCOR'$	α-Bromobenzylketone, $C_6H_5CHBrCOCH_2C_6H_5$	Ketoalcohol° [30]	Normal ester

Thus, the general nature of these transformations is determined by the additive tendency of the carbonyl group in the molecule of halogenated ketone, and the differences in the end products depend on the specific influences of the reagents acting.

The investigation is being continued.

EXPERIMENTAL

The preparation of α-bromodibenzylketone

The bromination of dibenzylketone was carried out with elementary bromine in a solution of carbon tetrachloride. We used 53 g of the ketone (with m.p. 34.5°), 13 ml of bromine, and 250 ml of CCl_4. The reaction was carried out with cooling by means of snow, and with stirring, while a current of CO_2 was passed through in order to remove HBr. The bromine was added slowly, in small drops, in a solution of CCl_4 1:3 by volume. At the end of the reaction, the mixture was washed with a solution of $NaHCO_3$, then with water and dried over $CaCl_2$. The CCl_4 was removed under reduced pressure with gentle heating on the water bath. Upon cooling to a

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° Under the action of aqueous alkali.

low temperature and rubbing with a glass stirring rod, the residue crystallized. The weight of crude product was 74 g. The bromoketone was recrystallized twice from ether, and then from absolute alcohol. Crystallization took place only upon vigorous rubbing with a glass stirring rod. 53 g of the ketone gave 37 g of the pure bromoketone (yield 51%), m.p. 48-48.5° (data in the literature 48-50°, 43-44°, 49°) [7,34,35].

Analysis for halogen (bromine):
0.1917 g substance: 0.1253 g AgBr.
Found %: Br 27.80.
$C_{15}H_{13}OBr$. Computed %: Br 27.64.

An attempt was made to separate the bromoketone from the alcoholic and ethereal mother liquors by evaporating the solvent off on the water bath. This resulted in a considerable deepening of the color until it became dark red, and the oil which remained could not be made to crystallize by any method.

Investigation of the Reaction of α-Bromoketone with Potassium Acetate

Experiment I. We used 14 g of bromoketone (1 mole) and 15 g of potassium acetate (3 moles). The reaction was carried out in glacial acetic acid (100 g) which was heated on the water bath and stirred. The reaction was continued for 3 hours, until there was no further reaction for halogen. The liquid was poured off from the KBr precipitate, and the acetic acid was driven off in vacuum with gentle heating on the water bath. The residue was treated with water and extracted with ether.* The ether was driven off on the water bath. The last traces of ether were removed in vacuum, with heating to 60°. There remained a thick, viscous, reddish-orange oil, with a pleasant, fruity odor. It was impossible to crystallize the acetate by any method used. When an attempt was made to distil the acetate in vacuum, decomposition was observed. The analysis for carbon and hydrogen was therefore carried out on the crude product:

0.1330 g substance: 0.3704 g CO_2; 0.0731 g H_2O.
0.1484 g substance: 0.4123 g CO_2; 0.0800 g H_2O.
Found %: C 76.00, 75.80; H 6.20, 6.05.
$C_{17}H_{16}O_3$. Computed %: C 76.10; H 6.01.

The Action of CH_3MgBr on the Acetate

The Grignard reagent was prepared by passing CH_3Br into ether with 12 g of Mg. The crude (undistilled) acetate (15 g) was added to the ether solution with cooling. After the addition of the acetate, the reaction flask was heated to 40° for 4 hours. Then the magnesium-organic complex was decomposed, with cooling, by the addition of water. The ether layer was decanted and the magnesium salt washed with ether. The ether extract was dried over Na_2SO_4. The ether and the trimethylcarbinol formed in the reaction were drawn off in vacuum. The residue, after standing in a vacuum for 3 days, crystallized.

The glycol obtained was very soluble in the cold in methyl and ethyl alcohols, in acetone, benzene, and in ether. It dissolved in petroleum ether and in CCl_4 only upon heating.

After recrystallization from a mixture of CCl_4, benzene, and petroleum ether, it was in the form of a white powder with m.p. 86.5-87.5°.

0.1137 g substance: 0.3274 g CO_2; 0.0765 g H_2O.
0.1184 g substance: 0.3426 g CO_2; 0.0826 g H_2O.
Found %: C 78.60, 79.00; H 7.50, 7.80.
$C_{16}H_{18}O_2$. Computed %: C 79.25; H 7.49.

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* The ether extract was washed with Na_2CO_3 and with water, and dried with Na_2SO_4.

The mother liquor left after the removal of the solvent did not form crystals.

The Compound of Crystallization of the Glycol and Benzene

When an attempt was made to recrystallize the glycol from benzene, a molecular compound of the glycol and benzene was obtained. This appeared to be a mass of small white needles, matted into felt. The substance was carefully dried in a vacuum desiccator. When the melting point was determined, the substance was seen to form liquid at 60.5°, and finally to melt at 85.5°.

When the substance was dried in a desiccator at 90° for 1 hour, it lost 18.3% of its weight. During the following night, there was no change in weight on standing in a vacuum desiccator. An additional period of drying of 2 hours at 85° raised the loss of weight to 20.6%; heating for 2 more hours at 110°-130° brought the loss of weight up to 21.9%.

Computed %: C_6H_6 in $C_{16}H_{18}O_2 \cdot C_6H_6$: 24.4%.

Thus, the compound was very unstable, but the last traces of benzene could be removed only with great difficulty.

When the molecular compound was recrystallized from CCl_4 or a mixture of CCl_4 and petroleum ether, the glycol was obtained with m.p. 86.5-87.5°.

Experiment II. The acetate was obtained from the bromoketone by the action of anhydrous potassium acetate in absolute alcohol medium. 30 g of the bromoketone was used with 15 g of potassium acetate in 75 g of absolute alcohol. The reaction took place in 15 minutes. The alcohol was driven off and the residue treated with water, then extracted with ether. The ether extract was washed with $NaHCO_3$ and dried over Na_2SO_4. The compound distilled at b.p. 195-195.5° under 6 mm pressure, with partial decomposition and tarring. 22 g (74%) were obtained.

0.1343 g substance: 0.3717 g CO_2; 0.0706 g H_2O.
0.1430 g substance: 0.3955 g CO_2; 0.0760 g H_2O.
Found %: C 75.50, 75.50; H 5.90, 6.00.
$C_{17}H_{16}O_3$. Computed %: C 76.10; H 6.01.
n_α^{20} 1.5486; n_β^{20} 1.5661; d_4^{20} 1.129; d_4^0 1.147; MR_α 75.6; MR_β 77.5; $MR_{\alpha-\beta}$ 1.9.
$C_{17}H_{16}O_3F_6$. Computed: MR_α 74.71; MR_β 76.26.

This compound, with somewhat different constants, was obtained by Prevault and Sommer by the action of CH_3COONa on α-chlorodibenzylketone in acetic acid solution: b.p. 197° at 13 mm; d^{18} 1.1293; n_D^{18} 1.5526 [30].

The acetate was converted into the glycol by the action of CH_3MgBr (8 mole Grignard reagent per mole acetate). 20.5 g of the acetate were used for the reaction.

The glycol (15 g) did not crystallize, despite all attempts to make it do so. Then it was decided to transform it into a compound of crystallization with benzene. Upon heating with benzene, a crystalline product was actually obtained. After recrystallization from a mixture of petroleum ether and CCl_4, the glycol had m.p. 84.5-85.5°, and gave no lowering of the melting point when mixed with the glycol obtained from the acetate in the preceding experiment.

The Oxidation of the Glycol

a) The oxidation of the solid glycol. 3.5 g of the glycol (m.p. 86.5-87.5°) was dissolved in 25 ml of acetic acid. Then 1.6 g of chromic anhydride was added, all at once, in 15 ml of water. The reaction took place while stirring was continued for 1 hour. Then 100 ml of water was added, and the volatile products were distilled off until no more emulsion was formed. The solution was neutralized with Na_2CO_3. It was extracted with ether, and the extract dried over $CaCl_2$. The ether was driven off and the residue distilled. Fraction I came over at 68-75° at 11 mm and amounted to 1.6 g; Fraction II, the residue, amounted to 0.9 g.

The second fraction was treated with semicarbazide, and gave a semicarbazone, which corresponded to that of methylbenzylketone (judging from the m.p. of 178-180° and a mixed test). The first fraction was benzaldehyde, as upon standing in an open vessel for several days, it was converted into benzoic acid (m.p. 118°, mixed test 119-120°).

b) The oxidation of the liquid glycol . For the purpose of oxidation, 4.5 g of the uncrystallized portion of the glycol from Experiment I was used. The oxidation was carried out with 2.5 g of CrO_3 in the presence of 10.5 g of $KHSO_4$, in 50 ml of water, with stirring and gentle heating.

After the reaction had been completed, distillation was carried out directly from the reaction flask. The first drops of distillate were treated with a solution of semicarbazide. The semicarbazone which was obtained had a melting point after recrystallization of 201°, and a sample mixed with the semicarbazone of benzaldehyde melted at 201°.

The neutral product was extracted with ether. The ether was driven off and the residue distilled in vacuum from a small flask. Everything that could be distilled was driven off, up to 110° at 25 mm. The distillate was fractinnated. A fraction came over from 70 to 90° at 16 mm. This same fraction was distilled once more, and boiled within the limits 78-83° at 17 mm, i.e., its boiling point was lower than that of acetophenone would have been if the latter had been present among the products of oxidation (b.p. 83.5° at 12 mm).

The residue from the distillate (0.5 g), which did not boil up to 90° at 16 mm, was treated with a solution of semicarbazide. The precipitate which formed was washed with alcohol and ether, and recrystallized from hot alcohol. It melted at 181-182°. The melting point of a sample mixed with the semicarbazone of known methylbenzylketone was 181-182°. Thus, methylbenzylketone was found, and this indicated the structure of the glycol, which was a product of the normal reaction.

The neutral fraction (73-83° at 17 mm) after standing for a week in an open test tube, crystallized and was converted to benzoic acid, i.e., it was benzaldehyde (b.p. of benzaldehyde 60.6° at 10 mm).

The acid products of the oxidation were neutralized and concentrated by evaporation of the solvent. Acidification gave a crystalline acid, which was recrystallized and sublimed. Judging from the melting point and the absence of any lowering of the melting point when mixed with known benzoic acid, this was benzoic acid (m.p. 119.5-120°).

The results of the oxidation of the solid and liquid glycols made it evident that they were one and the same substance. As among the products of oxidation only methylbenzylketone and benzaldehyde were identified, while no acetophenone was found at all, the glycol was a single compound with the structure $C_6H_5CHOH \cdot COH(CH_3) \cdot CH_2C_6H_5$ (1,3-diphenyl-2-methylpropanediol-1,2). It is possible that the liquid product was a mixture of diasteroisomers.

Investigation of the reaction of the α-bromoketone with potassium benzoate

For the reaction we took 12 g of the α-bromoketone with m.p. 46-47°, 12 g of anhydrous potassium benzoate, and 75 g of absolute alcohol. The reaction was carried out with stirring and heating to 60°. After 2 hours, when the reaction mixture no longer showed the presence of halogen, the reaction was stopped and the mixture allowed to stand overnight.

After the usual treatment, the ethereal solution was dried over Na_2SO_4. When the ether was evaporated off, warty crystals were formed. The substance appeared to be very soluble in the cold in ether, acetone, toluene, and chloroform, and soluble upon heating in petroleum ether, ligroin, CCl_4, and ethyl alcohol.

The best solvent for recrystallization appeared to be CCl_4. After recrystallization, the m.p. was 82.5-83.5°.

0.1497 g substance: 0.4369 g CO_2; 0.0759 g H_2O.
0.1507 g substance: 0.4398 g CO_2; 0.0745 g H_2O.
Found %: C 79.60, 79.60; H 5.70, 5.50.
$C_{22}H_{18}O_3$. Computed %: C 80.00; H 5.49.

0.1364 g substance: 12.166 g benzene; Δt 0.205°.
0.1289 g substance: 12.166 g benzene; Δt 0.178°.
Found: M 281, 306.
$C_{22}H_{18}O_3$. Computed: M 330.

The main ether extract of the compound from the alcoholic solution was subjected to a slow fractional evaporation. This gave crystals which after recrystallization appeared to be the same compound, with m.p. 82.5-83.5°.

After the evaporation of the solvent in a vacuum desiccator, the mother liquor, which was in the form of a viscous mass, was transferred to a porous plate. This resulted in the separation of an almost white substance, which as far as melting point and a mixed melting point test were concerned, appeared to be identical with the main substance.

Thus, the entire product of the reaction appeared to be a single compound (m.p. 82.5-83.5°).

The Synthesis of the Isomeric Benzoate from α-Bromobenzylacetophenone

α-Bromobenzylacetophenone was obtained by the bromination of the ketone in ether solution. After recrystallization from methanol it melted at 55° (the literature gives as the melting point 57-59°, 56-57°, 50-51° [7,37,38]).

16.5 g of the bromoketone (1 mole) was heated with 17 g of potassium benzoate (1.8 mole) in 100 ml of absolute alcohol for 10.5 hours, until there was no further reaction for halogen. The alcohol was driven off and the residue treated with water, with a solution of potash, and again with water. It was then dried in vacuum. Weight 19 g. The crystalline residue was then recrystallized from ether. The solution was subjected to gradual concentration, giving several crops of crystals. All the fractions obtained had a melting point within the limits 106 to 110°, and gave no lowering of the melting point when mixed with each other. Extracts were made with various solvents for the purpose of removing a possible impurity, but in all cases (with petroleum ether, chloroform, and alcohol) the same substance was obtained.

The mother liquor was concentrated and recrystallized from ether, alcohol, and petroleum ether, while attempts were also made to fractionate it by precipitating crystals by gradual evaporation. In all experiments, the same substance with melting range of about 106 to 110° was also obtained.

After recrystallization from alcohol, the benzoate obtained had m.p. 109.5-110°. The benzoate was very soluble in the cold in ether and in acetone. In petroleum ether, ethyl alcohol, and chloroform, it dissolved only upon heating.

SUMMARY

1. It has been shown that the reaction between α-bromodibenzylketone and potassium acetate or potassium benzoate gives only the ester of normal structure.

2. A mechanism has been suggested for the substitution of the halogen in α-halogenated ketones by an ester residue.

3. Data have been listed to indicate the general nature of the reaction mechanisms between α-halogenated ketones with salts of carboxylic acids on the one hand, and with alkalies on the other.

In conclusion, the author wishes to utilize the occasion to express his profound thanks to Prof. T.I.Temnikova for her valuable guidance and cooperation in this work.

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DERIVATIVES OF ACETYLENE

113. The Mechanism of Hydration and Cyclization of Dienines; The Hydration and Cyclization of 1-Vinylethinyloctalins and of 1-Vinylethinyl 3 4 Dihydronaphthalene

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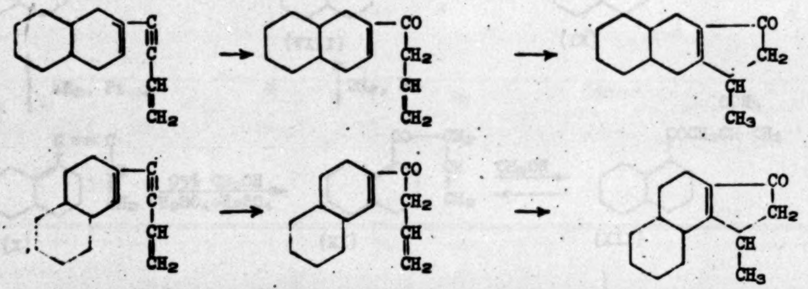
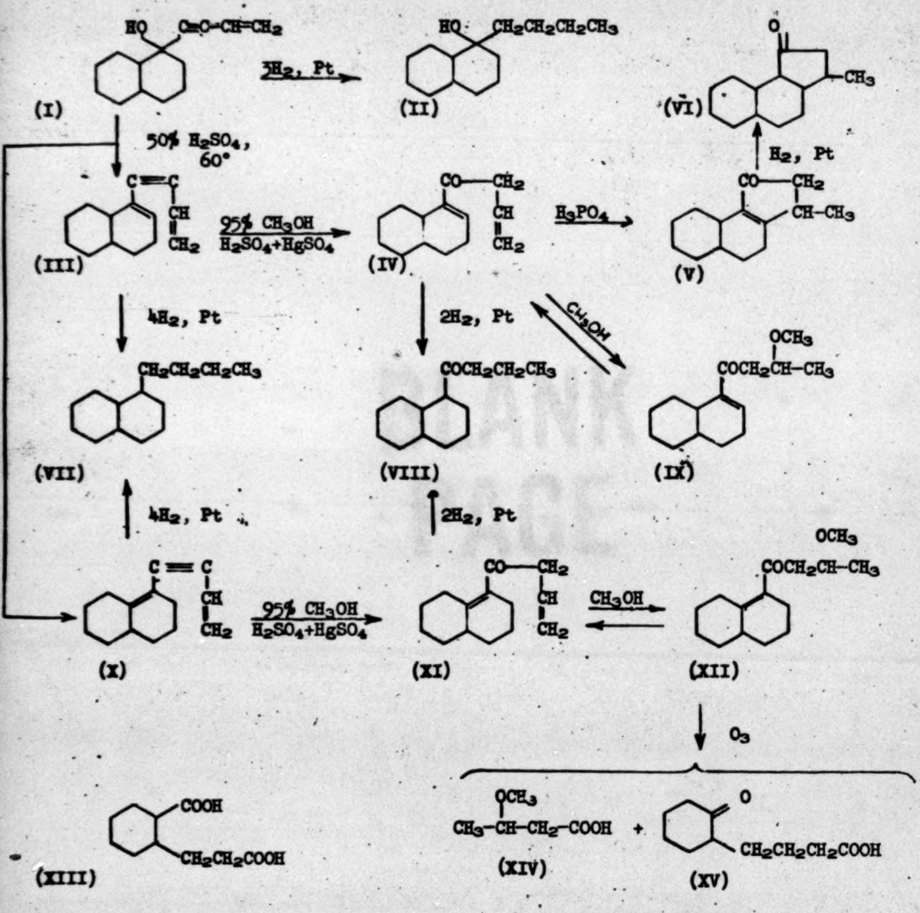
In one of our preceding communications [1] we described the hydration of 2-vinylethinyloctalins to give the corresponding allyl-2-octalyl ketones, and the cyclization of the latter to give tricyclic ketones, in the form of hydrogenated derivatives of methylbenzindanones:



It was thus shown that the reactions developed in our laboratory [2] for the hydration of dienines and the cyclization of the dienones corresponding to them to give cyclopentenones was completely applicable also to the synthesis of polycyclic systems containing the cyclopentenone nucleus.

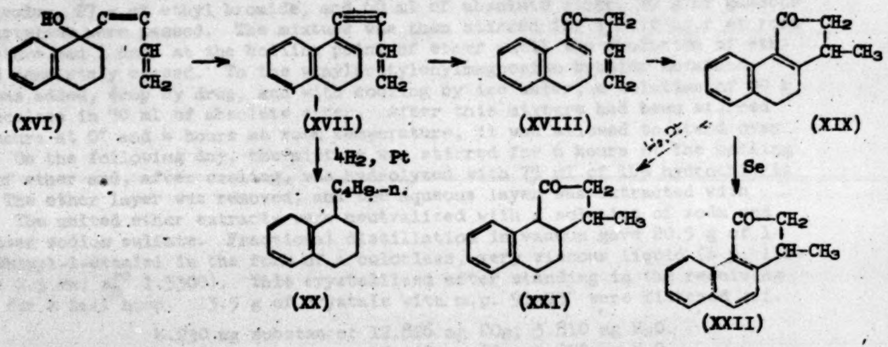
In the present work, further examples of the application of these reactions to the synthesis of polycyclic ketones are described. The action of vinylacetylenylmagnesium bromide on α-decalone, as well as the condensation of vinylacetylene with α-decalone in the presence of powdered caustic potash, gave a 75% yield of 1-vinylethinyl-1-decalol (I). When this was hydrogenated by means of Pt catalyst, it absorbed the three molecules of hydrogen required by theory, and gave 1-butyl-1-decalol (II). When the carbinol (I) was dehydrated by means of 50% sulfuric acid, an 80% yield of a mixture of 1-vinylethinyl-$\Delta^{1,2}$-octalin (III) and 1-vinylethinyl-$\Delta^{1,9}$-octalin (X) was obtained. When this was hydrogenated with Pt catalyst it absorbed 4 molecules of hydrogen and gave 1-butyldecalin (VII).

When the mixture of dienines (III and X) was hydrated in a solution of 95% aqueous methanol in the presence of sulfuric acid and mercury sulfate, it formed the corresponding mixture of allyl-α-$\Delta^{1,2}$-octalylketone (IV) and allyl-α-$\Delta^{1,9}$-octalylketone (XI). Under the conditions of hydration of the dienines (III and X), there were formed, along with the dienones (IV and XI) the corresponding


HO C≡C-CH=CH₂
(I)
3H₂, Pt
HO CH₂CH₂CH₂CH₃
(II)
O
CH₃
(VI)
50% H₂SO₄, 60°
H₂, Pt
C≡C
CH
CH₂
(III)
95% CH₃OH
H₂SO₄+HgSO₄
CO—CH₂
CH
CH₂
(IV)
H₃PO₄
CO—CH₂
CH-CH₃
(V)
4H₂, Pt
2H₂, Pt
CH₃OH
CH₂CH₂CH₂CH₃
(VII)
COCH₂CH₂CH₃
(VIII)
OCH₃
COCH₂CH-CH₃
(IX)
4H₂, Pt
2H₂, Pt
C≡C
CH
CH₂
(X)
95% CH₃OH
H₂SO₄+HgSO₄
CO—CH₂
CH
CH₂
(XI)
CH₃OH
OCH₃
COCH₂CH-CH₃
(XII)
O₃
COOH
CH₂CH₂COOH
(XIII)
OCH₃
CH₃-CH-CH₂-COOH
(XIV)
+
O
CH₂CH₂CH₂COOH
(XV)

methoxyketones (IX and XII). These were formed as a result of the addition of methanol to the allyl group in these dienones. In the most extended experiments on the hydration of the dienines (III and X) (above 5 hours) the methoxyketones (IX) and (XII) were the chief, or even the sole, products of the reaction.

The cleavage of methanol from the methoxyketones (IX and XII) by means of p-toluenesulfonic acid again gave the original dienones (IX and XI), which absorbed two molecules of hydrogen upon hydrogenation with Pt catalyst and gave propyl-α-decalylketone (VIII). The oxonation of the methoxyketones (IX and XII) gave β-methoxybutyric acid (XIV) and the γ-(2-ketocyclohexyl)-butyric acid (XV) which had previously been described by Huckel [3], corresponding to the methoxyketone (XII). From the residue of heavy oily acids obtained by the ozonation of the methoxyketones (IX and XII), it was impossible to isolate the β-(2-carboxycyclohexyl)-propionic acid (XIII), also described by Huckel [3], corresponding to the methoxyketone (IX). We were also unable to obtain this dicarboxylic acid (XIII) by the ozonation of the dienones (IV and XI). Despite the fact that we were unable by means of ozonation in this fashion to demonstrate directly the presence of the dienone (IV) and the methoxyketone (IX), the presence of these compounds among the products of the reaction could not be doubted, as dehydration of the carbinol (I) must have produced, in addition to the dienine (X), the dienine (III), the dehydration taking place in the same way as the dehydration of the other α-decalols [3]. When the dienones (IV and XI) were treated with phosphoric acid, a 30% yield of a tricyclic ketone was obtained. This had to be 3-methyl-$\Delta^{8,9}$-octahydro-6,7-benzindane-1-one (V), formed as a result of the cyclization of the dienone (IV). During this reaction, the rest of the substance was converted into a tar. This fact can be explained, in all probability, by the inability of the dienone (XI) to form a ring because of steric conditions, as the closing of this ring would have to take place at an angle. The tricyclic ketone (V) is also obtained in the same yield (30%) directly from the carbinol (I) or from the dienines (III and X) by treating them with phosphoric acid. In this case too a considerable part of the substance, corresponding to diene (X), is turned into a tar. The hydrogenation of the tricyclic ketone (V) with Pt catalyst gave the saturated tricyclic ketone (VI). Similar transformations were carried out starting with α-tetralone, upon which vinylacetylenylmagnesium bromide



acted to give immediately, in a 61% yield, 1-vinylethinyl-3,4-dihydronaphthalene (XVIII), which was formed by the dehydration of 1-vinylethinyl-1-tetralol (XVI) during the process of the synthesis itself. During the hydrogenation of the dienine (XVII) with Pt catalyst, 4 molecules of hydrogen were absorbed, and 1-butyltetralin (XX) was formed. The hydration of the dienine (XVII) in aqueous solutions of methanol in the presence of sulfuric acid and mercuric sulfate gave the dienone (XVIII), which, however, could not be isolated because of the fact that it completely underwent ring formation even under the conditions of its formation, to give the tricyclic ketone (XIX), which was 3-methyl-4,5-dihydro-6,7-benzindane-1-one. The hydrogenation of the tricyclic ketone (XIX) in the presence of Pt catalyst gave 3-methyl-6,7-benzohydrindane-1-one (XXI), and dehydrogenation of the tricyclic ketone (XIX) by means of selenium converted the latter into 3-methyl-6,7-benzindane-1-one (XXII).

EXPERIMENTAL

As the starting material for the preparation of α-decalone we used α-naphthol, which was exhaustively hydrogenated over Raney nickel in a solution of ethanol to give α-decalol [4,5,6,7]. Oxidation of the latter with chromic acid mixture gave α-decalone [8].

The Synthesis of 1-Vinylethinyl-1-decalol.

a) To 20 g of powdered caustic potash there was added 150 ml of dry ether. This was stirred continuously and cooled with a mixture of ice and salt (-5°), while a solution of 35 g of α-decalone and 20 g of vinylacetylene in 150 ml of dry ether was added drop by drop over a period of 40 minutes. The reaction mixture was then stirred for 3 hours at 0° and 3 hours at room temperature. On the following day, 100 ml of water was added to the reaction mixture during cooling with ice, and after energetic stirring, the ether layer was removed, and the aqueous layer extracted with ether. The united ether extracts were neutralized with 5% hydrochloric acid, dried over potash, and the residue, after removal of the ether, fractionated in vacuum. 35 g of 1-vinylethinyl-1-decalol (I) was obtained in the form of a viscous, colorless, transparent liquid:

B.p. 120-122° at 3 mm; n_D^{20} 1.5280; d_4^{20} 1.0035; MR found 62.65; computed 61.51.

5.342 mg substance: 16.100 mg CO_2; 4.670 mg H_2O.
Found %: C 82.25; H 9.78.
$C_{14}H_{20}O$. Computed %: C 82.25; H 9.87.

b) Through an ether solution of ethylmagnesium bromide, prepared from 5.4 g of magnesium, 27 g of ethyl bromide, and 60 ml of absolute ether, 20 g of gaseous vinylacetylene were passed. The mixture was then stirred for a half hour at room temperature and 1 hour at the boiling point of ether until the evolution of ethane had completely ceased. To the vinylacetylenylmagnesium bromide obtained there was added, drop by drop, and with cooling by ice water, a solution of 20 g of α-decalone in 50 ml of absolute ether. After this mixture had been stirred for 2 hours at 0° and 4 hours at room temperature, it was allowed to stand over night. On the following day, the mixture was stirred for 6 hours at the boiling point of ether and, after cooling, was hydrolyzed with 75 ml of 10% hydrochloric acid. The ether layer was removed, and the aqueous layer was extracted with ether. The united ether extracts were neutralized with a solution of soda and dried over sodium sulfate. Fractional distillation in vacuum gave 20.5 g of 1-vinylethinyl-1-decalol in the form of a colorless, very viscous liquid (b.p. 118-120° at 2.5 mm; n_D^{20} 1.5300). This crystallized after standing in the receiving vessel for a half hour. 13.5 g of crystals with m.p. 91-93° were filtered off.

4.230 mg substance: 12.826 mg CO_2; 3.810 mg H_2O.
4.355 mg substance: 13.192 mg CO_2; 3.920 mg H_2O.
Found %: C 82.75, 82.66; H 10.08, 10.07.
$C_{14}H_{20}O$. Computed %: C 82.25; H 9.89.

The Hydrogenation of 1-Vinylethinyl-1-decalol

4 g of the substance was hydrogenated in a solution of 20 ml of ethanol in the presence of platinum catalyst. For the hydrogenation of one triple and one double bond 1.32 liters of hydrogen were required. 1.35 liters were absorbed after an hour and a half of hydrogenation. Fractionation of the product of hydrogenation gave 3.5 g of 1-butyl-1-decalol (II) in the form of a very viscous, transparent, colorless liquid.

B.p. 110-112° at 2 mm; n_D^{20} 1.4942; d_4^{20} 0.9604.
Found MR 63.75; computed 63.97.

5.300 mg substance: 15.509 mg CO_2; 5.830 mg H_2O.
6.760 mg substance: 19.769 mg CO_2; 7.470 mg H_2O.
Found %: C 79.86, 79.80; H 12.31, 12.36.
$C_{14}H_{26}O$. Computed %: C 79.92; H 12.47.

The Dehydration of 1-Vinylethinyl-1-decalol

A mixture of 37 g of 1-vinylethinyl-1-decalol and 40 ml of 50% sulfuric acid was stirred energetically for 6 hours at 60° in the presence of a small quantity of pyrogallol. The hydrocarbon was extracted with ether, and the ether extract was neutralized with soda, dried over sodium sulfate, and distilled in vacuum. We obtained 27 g of a mixture of 1-vinylethinyloctalins (III and X) in the form of a mobile light yellow liquid:

B.p. 112-114° at 3 mm; n_D^{20} 1.5595; d_4^{20} 0.9605;
MR found 62.62; computed 59.51.

3.594 mg substance: 11.867 mg CO_2; 3.204 mg H_2O.
4.014 mg substance: 13.173 mg CO_2; 3.459 mg H_2O.
Found %: C 90.12, 89.54; H 9.97, 9.64.
$C_{14}H_{18}$. Computed %: C 90.25; H 9.75.

The Hydrogenation of the 1-Vinylethinyloctalins (III and X)

1.5 g of the substance was hydrogenated in a solution of 10 ml of glacial acetic acid in the presence of platinum catalyst. For the hydrogenation of two double bonds and one triple bond, 0.72 liter of hydrogen was required. After two and one half hours, 0.75 liter of hydrogen had been absorbed. The product of the reaction was diluted with water and extracted with ether. The ether extract was neutralized with a solution of soda, dried over sodium sulfate, and distilled. 1.25 g of 1-butyldecalin (VII) was obtained in the form of a colorless, very mobile liquid:

B.p. 99-100° at 3 mm; n_D^{20} 1.4790; d_4^{20} 0.8857; Found MR 62.20, computed 62.45.

4.515 mg substance: 14.293 mg CO_2; 5.548 mg H_2O.
5.770 mg substance; 18.243 mg CO_2; 6.328 mg H_2O.
Found %: C 86.37, 86.27; H 13.50, 13.43.
$C_{14}H_{26}$. Computed %: C 86.51; H 13.50.

The Hydration of the 1-Vinylethinyloctalins

a) A mixture of 110 g of 95% methanol, 0.4 ml of concentrated sulfuric acid, 5 g of mercuric sulfate, and 18 g of 1-vinylethinyloctalins (III and X) was stirred for 1 hour at 60°. Most of the methanol was distilled off under a slight vacuum at a bath temperature of 60° over a period of 15 minutes. The residue was extracted with ether, and the ether extract was neturalized with a solution of soda, dried over sodium sulfate, and distilled. 15 g of a mixture of allyl-α-octalylketones (IV and XI) with β-methoxypropyl-α-octalylketones (IX and XII) was obtained. Boiling range 125-142° at 4 mm; n_D^{20} 1.5248.

b) 20 g of 1-vinylethinyloctalins, 120 g of 95% methanol, 0.4 ml of concentrated sulfuric acid, and 6 g of mercuric sulfate were stirred for 6½ hours at 60°. Most of the methanol was distilled off under a slight vacuum at a bath temperature of 60° over a period of 20 minutes. The residue was extracted with ether, and the ether extract neutralized with a solution of soda, dired over sodium sulfate, and fractionated in vacuum. 16.5 g of β-methoxypropyl-α-octalylketones (IX and XII) were obtained in the form of a yellow, transparent mobile liquid:

B.p. 128-130° at 2 mm; n_D^{20} 1.5100; d_4^{20} 1.019;
Found MR 69.27, computed 68.25.

5.080 mg substance: 14.543 mg CO_2; 4.481 mg H_2O.
3.700 mg substance; 10.581 mg CO_2; 3.280 mg H_2O.
Found %: C 78.14, 78.04; H 9.89, 9.92.
$C_{15}H_{24}O_2$. Computed %: C 76.25; H 10.24.

The Cleavage of Methanol from the Methoxyketones (IX and XII)

To 15 g of the methoxyketone, 0.05 g of p-toluenesulfonic acid was added, and the mixture was heated at a pressure of 100 mm at 130-135° for 25 minutes. The substance was then distilled under the vacuum of an oil pump. 12.5 g of a mixture of allyl-α-octalylketones (IV and XI) were obtained in the form of a mobile, light yellow liquid:

B.p. 121-123° at 3 mm; n_D^{20} 1.5220; d_4^{20} 0.9984;
Found MR 62.35, computed 61.53.

7.944 mg substance: 23.949 mg CO_2; 7.084 mg H_2O.
4.863 mg substance: 14.704 mg CO_2; 4.265 mg H_2O.
Found %: C 82.27, 82.25; H 9.98, 9.81.
$C_{14}H_{20}O$. Computed %: C 82.25; H 9.87.

The Hydrogenation of Allyl-α-octalylketones (IV and XI)

a) 3.2 g of the material was hydrogenated in 10 ml of acetic acid in the presence of platinum catalyst. For the hydrogenation of two double bonds, 0.7 liter of hydrogen was required; after 14 hours of hydrogenation, 0.65 liter of hydrogen had been absorbed. The catalyst was filtered off, and the product was neutralized with a solution of alkali, and extracted with ether. The ether extract was dried over sodium sulfate and fractionated. 1.8 g of propyl-α-decalylketone (VIII) was obtained in the form of a colorless, mobile liquid:

B.p. 93.5-94.5° at 2.5 mm; n_D^{20} 1.4840; d_4^{20} 0.9496;
Found MR 62.67; computed 62.46.

10.35 mg substance; 30.60 mg CO_2; 10.09 mg H_2O.
18.07 mg substance: 53.47 mg CO_2; 17.61 mg H_2O.
Found %: C 80.68, 80.75; H 10.92, 10.91.
$C_{14}H_{24}O$. Computed %: C 80.70; H 11.62.

b) 2 g of the material was hydrogenated in a solution of 15 ml of ethanol in the presence of platinum catalyst. For the hydrogenation of two double bonds, 0.44 liter hydrogen was required; after the first hour and a half of hydrogenation, 0.4 liter had been absorbed, after 12 more hours, 0.05 liter more of hydrogen. The catalyst was filtered off, and after the ethanol had been driven off, the residue was fractionated in vacuum. 1.2 g of material was obtained.

B.p. 119-120° at 3.5 mm; n_D^{20} 1.4950; d_4^{20} 0.9670; MR Found 62.73, Computed 62.46.

5.140 mg substance: 15.305 mg CO_2; 5.120 mg H_2O.
5.530 mg substance: 16.507 mg CO_2; 5.600 mg H_2O.
Found %: C 81.26, 81.46; H 11.13, 11.33.
$C_{14}H_{24}O$. Computed %: C 80.70; H 11.62.

The Ozonation of the β-Methoxypropyl-α-octalylketones (IX and XII)

Ozonized oxygen was passed for 12 hours through a solution of 10 g of the substance in 35 ml of dry chloroform with a velocity of 4 to 5 liters per hour (concentration of ozone 5%). To the solution of the ozonide, 35 ml of water was added, and the mixture was stirred for 4 hours at room temperature and then allowed to stand overnight. On the following day, 8 ml of 40% hydrogen peroxide was added, and the mixture was stirred at 60° for 7 hours. The product was neutralized with soda (9.5 g), the chloroform layer was removed, and the aqueous layer was extracted with ether. After the ether and chloroform had been driven off, 0.3 g of neutral products was obtained. This was not investigated further. In the aqueous salt solution only traces of formic acid were detected by the calomel method. The salt solution was evaporated to dryness in vacuum, the residue acidified with concentrated hydrochloric acid (25 ml), and the organic acids extracted with ether, dried over sodium sulfate, and fractionated in vacuum. 1 g of β-methoxybutyric acid was obtained, b.p. 105-110° at 9 mm and 209-213° at normal pressure; n_D^{20} 1.4206. After the β-methoxybutyric acid had been distilled off in vacuum, there remained 4 g of a mixture of acids, in the form of a viscous, dark oil. This oil gave the semicarbazone of γ-2-ketocyclohexylbutyric acid with m.p. 187-188° (from methanol) [3].

2.250 mg substance: 0.497 ml N_2 (17°, 746 mm).
Found %: N 17.43.
$C_{11}H_{19}O_3N_3$. Computed %: N 17.93.

The decomposition of this semicarbazone by boiling with 2 N sulfuric acid gave γ-2-ketocyclohexylbutyric acid (XV) itself, m.p. 56-57.5° (from carbon tetrachloride and petroleum ether). This agreed with the data of Huckel [3]. The thick oil obtained after the separation of the semicarbazone of the keto acid (XV) did not crystallize either upon prolonged standing or on cooling, and it was impossible to isolate the β-(2-carboxycyclohexyl)-propionic acid it contained. The silver salts, obtained by fractional precipitation from this oil, decomposed while they were being obtained, and it was impossible to analyze them.

Similar results were also obtained by the ozonation of the dienones (IV and XI). This resulted in the separation of formic acid in an amount 56.5% of the theoretical, and in the formation of a mixture of acids in the form of a viscous oil which could not be made to crystallize. The silver salts from this mixture decomposed as they were formed, and it was impossible to carry out their analysis.

The Transformation of 1-Vinylethinyl-1-decalol into 3-Methyl-$\Delta^{8,9}$-octahydro-6,7-benzindane-1-one

A mixture of 30 g of 1-vinylethinyl-1-decalol with 30 ml of phosphoric acid (sp. gr. 1.83) was stirred for 6.5 hours at 65°. The product was dissolved in ether, neutralized with a solution of soda, dried over sodium sulfate, and fractionated in vacuum. 9 g of 3-methyl-$\Delta^{8,9}$-octahydro-6,7-benzindane-1-one (V) was obtained in the form of a colorless viscous liquid with a camphor odor:

B.p. 128-130° at 2 mm; n_D^{20} 1.5300; d_4^{20} 1.043.
MR Found 60.48; computed 59.80.

5.222 mg substance; 15.747 mg CO_2; 4.627 mg H_2O.
4.855 mg substance: 14.600 mg CO_2; 4.300 mg H_2O.
Found %: C 82.27, 82.07; H 9.81, 9.91.
$C_{14}H_{20}O$. Computed %: C 82.25; H 9.87.

The 2,4-dinitrophenylhydrazone melted at 112-114° (from methanol):

4.502 mg substance: 0.578 ml N_2 (24°, 738 mm).
3.485 mg substance: 0.443 ml N_2 (24°, 739 mm).
Found %: N 14.33, 14.21.
$C_{20}H_{24}O_4N_4$. Computed %: N 14.57.

We could not obtain a crystalline semicarbazone.

The Hydrogenation of 3-Methyl-$\Delta^{8,9}$-octahydro-6,7-benzindane-1-one

3 g of the substance was hydrogenated in a solution of 10 ml of glacial acetic acid in the presence of platinum catalyst. For the hydrogenation of one double bond, 0.33 liter of hydrogen was required; after 2 hours of hydrogenation, 0.34 liter had been absorbed. The catalyst was filtered off, and the mixture diluted with water and extracted with ether. The ether extract was neutralized with a solution of soda, dried over sodium sulfate, and the residue, after the ether had been removed, was distilled in vacuum. 2.5 g of 3-methyldecahydro-6,7-benzindane-1-one (VI) was obtained in the form of a viscous, colorless liquid:

B.p. 114-116° at 2 mm; n_D^{20} 1.5120; d_4^{20} 1.025;
MR found 60.37, computed 60.26.

5.375 mg substance: 16.100 mg CO_2; 5.135 mg H_2O.
5.470 mg substance: 16.360 mg CO_2; 5.257 mg H_2O.
Found %: C 81.61, 81.74; H 10.75, 10.69.
$C_{14}H_{20}O$. Computed %: C 81.46; H 10.75.

The semicarbazone melted at 205-206.5° (from methanol):

3.930 mg substance: 0.521 ml N_2 (24°, 743 mm).
3.230 mg substance: 0.439 ml N_2 (24°, 743 mm).
Found %: N 14.90, 15.27.
$C_{15}H_{25}ON_3$. Computed %: N 15.05.

The 2,4-dinitrophenylhydrazone melted at 147-149° (from methanol).

3.360 mg substance: 0.414 ml N_2 (24°, 741 mm).
3.990 mg substance: 0.485 ml N_2 (24°, 741 mm).
Found %: N 13.81, 13.62.
$C_{20}H_{28}O_4N_4$. Computed %: N 14.50.

The Cyclization of the 1-Vinylethinyloctalins

A mixture of 5 g of the 1-vinylethinyloctalins (III and X) and 5 ml of phosphoric acid (sp. gr. 1.75) was stirred for 7 hours at 65°. The product was dissolved in ether, neutralized with a solution of soda, and dried over sodium sulfate. A vacuum distillation gave 1.8 g of 3-methyl-$\Delta^{8,9}$-octahydro-6,7-benzindane-1-one (V), in the form of a viscous, colorless liquid with a camphor odor. B.p. 120-123° at 1 mm; n_D^{20} 1.5310. The 2,4-dinitrophenylhydrazone melted at 110-114°, and a mixed test with the sample described above showed no lowering.

The Cyclization of the Allyl-α-octalylketones

A mixture of 5 g of the allyl-α-octalylketones (IV and XI) and 5 ml of phosphoric acid (sp. gr. 1.70) was stirred for 6.5 hours at 60-65°. The product was dissolved in ether, neutralized with a solution of soda, and dried over sodium sulfate. A vacuum distillation gave 1.5 g of 3-methyl-$\Delta^{8,9}$-octahydro-6,7-benzindane-1-one (V) in the form of a viscous, colorless liquid with a camphor odor; b.p. 132-135° at 3 mm; n_D^{20} 1.5265; Its 2,4-dinitrophenylhydrazone melted at 112-115°, and gave no lowering when mixed with the sample described above, obtained from 1-vinylethinyl-1-decalol.

The Oxidation of Tetralin to Give α-Tetralone

To a solution of 80 g of tetralin in 480 ml of glacial acetic acid, a mixture of 150 g of chromic anhydride, 75 ml of water, and 400 ml of glacial acetic acid was added over a period of one hour, with vigorous stirring, and cooling with ice. The reaction mixture was then stirred for 3 hours at 12°, and allowed to stand for 5 days at room temperature. The acetic acid was distilled off under a slight vacuum at a bath temperature of 40-45°, and the residue was extracted with ether, neutralized with a solution of soda, dried over magnesium sulfate, and distilled. 55 g of α-tetralone was obtained; b.p. 122-127° at 10 mm; n_D^{20} 1.5710.

The Synthesis of Vinylethinyl-3,4-dihydronaphthalene

To the vinylacetylenylmagnesium bromide prepared from 7.2 g of magnesium, 36 g of ethyl bromide, 21 g of vinylacetylene, and 80 ml of ether, there was added over a period of an hour, with continuous stirring and cooling with ice water, a solution of 29.2 g of α-tetralone in 200 ml of absolute ether. After the first third of the ketone solution had been added, the reaction mixture became noticeably more viscous, and toward the end of the addition of the ether it was a thick rose-colored mass, difficult to stir with the mechanical stirrer. After all of the ketone solution had been added, the reaction mixture was stirred for another 3 hours at room temperature, and allowed to stand overnight. On the following day, the reaction mixture was cooled with ice, and there was added to it first 10 ml of water and then 100 ml of 10% hydrochloric acid. The ether layer was drawn off, and the aqueous layer was extracted with ether. The united ether extracts were neutralized with a solution of soda and dried over sodium sulfate. After the ether had been driven off, the residue was distilled in vacuum. It gave 22 g of 1-vinylethinyl-3,4-dihydronaphthalene (XVII) in the form of a mobile, light yellow liquid:

B.p. 125-127° at 3 mm; n_D^{20} 1.6240; d_4^{20} 1.027;
MR found 61.88; computed 58.11.

7.020 mg substance: 23.804 mg CO_2; 4.350 mg H_2O.
4.080 mg substance: 13.847 mg CO_2; 2.532 mg H_2O.
Found %: C 92.54, 92.62; H 6.93, 6.94.
$C_{14}H_{12}$. Computed %: C 93.22; H 6.78.

The Hydrogenation of 1-Vinylethinyl-3,4-dihydronaphthalene

3.6 g of the substance was hydrogenated in a solution of 10 ml of glacial acetic acid over platinum catalyst. 2 liters of hydrogen was absorbed; 1.8 liters of hydrogen was required for the hydrogenation of two double bonds and one triple bond. The acetic acid was driven off under a slight vacuum, and the residue extracted with ether, neutralized with a solution of soda, and dried over sodium sulfate. A distillation of the product of hydrogenation in vacuum gave 2.6 g of 1-butyltetralin (XX) in the form of a very mobile, colorless liquid.

B.p. 120-121° at 7 mm; n_D^{20} 1.5210; d_4^{20} 0.9400.
MR found 60.90; computed 61.05.

4.470 mg substance: 14.602 mg CO_2; 4.290 mg H_2O.
4.787 mg substance: 15.644 mg CO_2; 4.557 mg H_2O.
Found %: C 89.15, 89.18; H 10.74, 10.65.
$C_{14}H_{20}$. Computed %: C 89.29; H 10.71.

The Hydration of 1-Vinylethinyl-3,4-dihydronaphthalene

A mixture of 85 ml of 95% methanol, 1.4 ml of concentrated sulfuric acid, 5 g of mercuric sulfate, and 8.5 g of the hydrocarbon (XVII) was stirred at 55-60° for 10 hours. Most of the methanol was driven off under a slight vacuum at a bath temperature of 60° over a period of 20 minutes. The residue was extracted with ether, neutralized with a solution of soda, and dried over sodium sulfate. After the ether had been driven off on the water bath, the substance crystallized. 4.5 g of 3-methyl-4,5-dihydro-6,7-benzindane-1-one (XIX) was obtained; m.p. 90-91.5° (from methanol).

5.920 mg substance: 18.409 mg CO_2; 3.547 mg H_2O.
4.980 mg substance: 15.517 mg CO_2; 2.970 mg H_2O.
Found %: C 84.86, 85.03; H 6.70, 6.67.
$C_{14}H_{14}O$. Computed %: C 84.80; H 7.12.

The semicarbazone precipitated after more than a day from a mixture containing the original substance, from which it was purified by boiling with petroleum ether. M.p. 162-164° (from ethanol).

4.520 mg substance: 0.631 ml N_2 (18°, 745 mm).
3.500 mg substance: 0.498 ml N_2 (21°, 746 mm).
Found %: N 16.06, 16.21.
$C_{15}H_{17}ON_3$. Computed %: N 16.45.

The 2,4-dinitrophenylhydrazone melted at 238-239° (from methanol).

4.185 mg substance: 0.552 ml N_2 (26°, 747 mm).
4.320 mg substance: 0.565 ml N_2 (25°, 747 mm).
Found %: N 14.80, 14.73.
$C_{20}H_{18}O_4N_4$. Computed %: N 14.79.

The dihydrobenzindanone (XIX) remained unchanged after 5 hours of heating at 65° with phosphoric acid (sp. gr. 1.85).

The Hydrogenation of 3-Methyl-4,5-dihydro-6,7-benzindane-1-one

1.2 g of the substance (m.p. 90-91°) was hydrogenated in a solution of 10 ml of glacial acetic acid, in the presence of platinum catalyst. For the hydrogenation of one double bond, 0.13 liter of hydrogen was required; after 54 hours of shaking, 0.14 liter of hydrogen had been absorbed. The mixture was diluted with water, neutralized with soda, and extracted with ether. The ether extract was dried over sodium sulfate, and distilled. 0.8 g of material was obtained (b.p. 130-153° at 3 mm; n_D^{20} 1.5872). From this, the semicarbazone of the tricyclic ketone (XXI) was obtained, with m.p. 207-209° (from methanol).

4.780 mg substance: 0.666 ml N_2 (21°, 751 mm).
3.040 mg substance: 0.428 ml N_2 (22°, 751 mm).
Found %: N 16.00, 16.09.
$C_{15}H_{19}ON_3$. Computed %: N 16.36.

A mixed test with the semicarbazone of the original 3-methyl-4,5-dihydro-6,7-benzindane-1-one melted at 160-162°.

The Dehydrogenation of 3-Methyl-4,5-dihydro-6,7-benzindane-1-one

1.5 g of the substance (m.p. 90-92°) was heated in a small Wurtz flask with 3 g of metallic selenium. The evolution of hydrogen selenide began at 208°. A total of 12 ml of gas was evolved. The heating was continued for 2 hours at 200 to 280°. The transparent oil was dissolved in ether, neutralized with a solution of soda, and dried over sodium sulfate. The ether was driven off and the residue crystallized. 1.4 g of crystals with m.p. 75-77° (from petroleum ether) was obtained. A mixed test with the original 3-methyl-4,5-dihydro-6,7-benzindane-1-one melted at 83-87°.

4.580 mg substance: 14.220 mg CO_2; 2.592 mg H_2O.
4.438 mg substance: 13.777 mg CO_2; 2.495 mg H_2O.
Found %: C 84.73, 84.72; H 6.32, 6.29.
$C_{14}H_{12}O$. Computed %: C 85.67; H 6.17.

The 2,4-dinitrophenylhydrazone had m.p. 255-258° (from methanol).

3.090 mg substance: 0.371 ml N_2 (26°, 750 mm).
3.370 mg substance: 0.411 ml N_2 (26°, 750 mm).
Found %: N 13.53, 13.74.
$C_{20}H_{16}O_4N_4$. Computed %: N 14.89.

A mixed test of the 2,4-dinitrophenylhydrazone with that of the original 3-methyl-4,5-dihydro-6,7-benzindane-1-one melted at 232-237°.

SUMMARY

The action of vinylacetylenylmagnesium bromide upon α-decalone gave 1-vinylethinyl-1-decalol (I) in 75% yield. When this was dehydrated with 50% sulfuric acid, it formed a mixture of 1-vinylethinyloctalins (III and X). When the dienines (III and X) were hydrated in aqueous solutions of methanol, in the presence of sulfuric acid and mercuric sulfate, they formed the corresponding mixture of allyl-α-octalylketones (IV and XI) and methoxyketones (IX and XII). Methanol was split off from the methoxyketones (IX and XII) by means of p-toluenesulfonic acid to regenerate the original dienones (IV and XI). Upon treatment with phosphoric acid these gave a 30% yield of the tricyclic ketone (V), which was formed by the cyclization of the dienone (IV) according to the usual manner. The isomeric dienone (XI) was apparently incapable of cyclization because of steric factors (the closure of the ring would have had to take place at an angle), and was completely converted into a tar during the reaction.

The action of vinylacetylenylmagnesium bromide on α-tetralone gave the diene (XVII) directly in a yield of 61%. This was formed by the dehydration of the carbinol (XVI) during its synthesis. When the dienine (XVII) was hydrated under the usual conditions, it at once gave the tricyclic ketone (XIX), and it was impossible to isolate the intermediate dienone (XVIII) during the reaction, as the latter underwent ring-formation completely under the conditions of its formation.

The hydrogenation of the products obtained to give the corresponding saturated compounds has been described.

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INVESTIGATIONS IN THE DOMAIN OF THE SYNTHESIS AND TRANSFORMATION OF o-HALOGENETHYL ALKYL ETHERS

II. α-BROMOETHYL ALKYL ETHERS

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The increased ability of the double bond in the molecules of vinyl alkyl ethers to form addition compounds is a result of the fact that it is located close to an oxygen atom. This property of the double bond in these compounds is in complete agreement with the catalytic role of the H ion in the transformations of vinyl alkyl ethers. Therefore the addition of hydrogen halide to the vinyl ethers is a form of reaction which permits us to determine the probable mechanism of the catalytic influence of the hydrogen halides in the processes involved in the transformation of the vinyl ethers.

The interaction of hydrogen bromide with vinyl ethers made it possible for us to develop a useful method for the preparation of both α-chloro- [1] and α-bromoethyl alkyl ethers, which takes place according to the following equation:

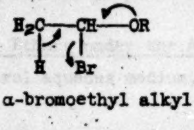
$$CH_2 = CH - OR + HBr \longrightarrow CH_3 - CHBr - OR.$$

α-Bromoethyl alkylethers are compounds which have hardly been investigated. Only a single work by Henry [2] gives the boiling point and specific gravity of α-bromodiethyl ether, obtained by him by the method of Wurtz and Frappoli [3].

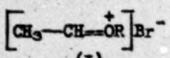
The structure of the α-bromoethyl alkyl ethers is of interest because of the differences between the molecular refractions found by us and those calculated. This is shown in the following table:

Formula of ether	MR_D found	MR_D calculated	Δ
$CH_3—CHBr—OCH_3$	26.11	25.46	0.65
$CH_3—CHBr—OC_2H_5$	31.94	30.08	1.86
$CH_3—CHBr—OC_4H_9$	40.08	39.31	0.77

The presence of this sort of exaltation in α-bromoethyl alkyl ethers, and their ability to undergo extraordinarily varied reactions permit us to assume that the following isomeric effects are present in these compounds:



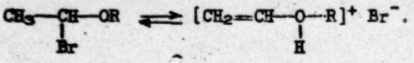
this permits us to picture the α-bromoethyl alkyl ethers as having the following oxonium structure.



$$\left[CH_3-CH=\overset{+}{O}R\right]Br^-$$

(I)

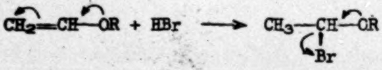
From this picture of the structure of α-bromoethyl alkyl ethers, we may assume the existence of the following tautomers:



$$\underset{\displaystyle Br}{CH_3-\underset{|}{CH}-OR} \rightleftharpoons [CH_2=CH-\underset{\displaystyle H}{\underset{|}{O}}-R]^+ Br^-.$$

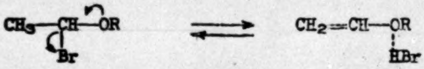
(II) (III)

The possibility of the existence of these tautomers is borne out by the method of preparation of these compounds:



$$CH_2=CH-OR + HBr \longrightarrow CH_3-\underset{\displaystyle Br}{\underset{|}{CH}}-OR$$

and there can be a further shift of the hydrogen, similar to what takes place in the enolization of ketones, to give an oxonium structure with a hydrogen bond:

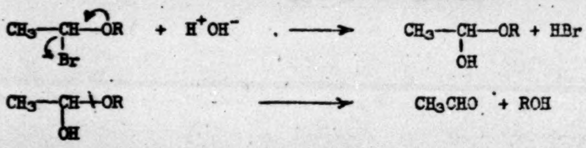


$$CH_3-\underset{\displaystyle Br}{\underset{|}{CH}}-OR \rightleftharpoons CH_2=CH-\underset{\displaystyle HBr}{\underset{\vdots}{O}}R$$

From this point of view, the catalytic role of these compounds in the transformations of vinylethers becomes comprehensible. It explains the ease with which H ions are split off from them.

Hence it is possible to explain the great ease and speed of addition to vinyl ethers of water, alcohols, and other compounds with a mobile hydrogen, which is observed in the presence of traces of hydrogen halide acids, [4].

The ionic character of the reaction follows from the speed at which it takes place, and as an example of hydrolysis, we can give the following sketch:



$$CH_3-\underset{\displaystyle Br}{\underset{|}{CH}}-OR + H^+OH^- \longrightarrow CH_3-\underset{\displaystyle OH}{\underset{|}{CH}}-OR + HBr$$

$$CH_3-\underset{\displaystyle OH}{\underset{|}{CH}}-OR \longrightarrow CH_3CHO + ROH$$

From this same reaction we can draw conclusions about the mechanism of the catalytic influence of mineral acids on vinyl alkyl ethers:

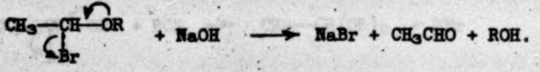
$$CH_2=CH-OR + H_2O \xrightarrow{H^+} CH_3CHO + ROH.$$

which ends in the formation of the ion $[CH_3-CH--OR]^+$ and the subsequent addition of the hydroxyl of water.

In our present investigation, we were interested in the properties of the α-bromine from the point of view of its position in the molecule of α-bromo ether. With this object in mind, we investigated the properties of these compounds with regard to the following reactions.

1. The Cleavage of α-Bromoethyl Ethers under the Action of Aqueous Alkali

In this case, as also in a neutral aqueous medium, hydrolysis takes place according to the following scheme:



$$CH_3—\underset{Br}{CH}—OR + NaOH \longrightarrow NaBr + CH_3CHO + ROH.$$

Under these conditions, hydrolysis takes place with the speed of neutralization.

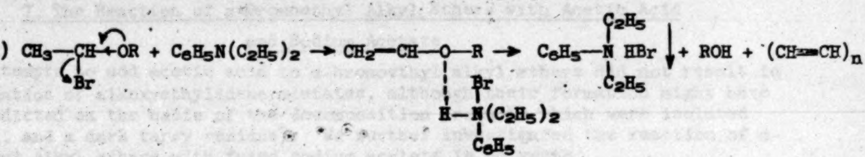
2. The Titration of the Bromine, by Volhard's Method

The quantitative determination of the bromine by Volhard's method in α-bromoethyl alkyl ethers confirms the ionic condition of the α-bromine in them.

3. The Interaction of α-Bromoethyl Alkyl Ethers and Diethylaniline

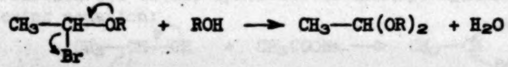
By means of this reaction applied to α-chloroethyl alkyl ethers, it was possible to demonstrate the change from α-chloroethyl alkyl ethers to the original vinyl alkyl ethers. In the case of α-bromoethyl alkyl ethers, however, this reaction took place differently. In the latter case, we observed the formation of acetals, which can be explained by the following equations:

a)



$$CH_3—\underset{Br}{CH}—OR + C_6H_5N(C_2H_5)_2 \rightarrow CH_2—CH—\underset{\underset{\underset{C_6H_5}{H—N(C_2H_5)_2}}{Br}}{O}—R \rightarrow C_6H_5—\underset{C_2H_5}{\overset{C_2H_5}{N}}\,HBr\downarrow + ROH + (CH{\equiv}CH)_n$$

b)



$$CH_3—\underset{Br}{CH}—OR + ROH \longrightarrow CH_3—CH(OR)_2 + H_2O$$

In general, we must note that in the presence of the H ion, we observed decomposition, with the formation of acetals and tar, formed probably on account of the acetylene portion of the molecule of vinyl ether.

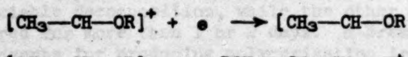
4. The Action of Ammonia on α-Bromoethyl Alkyl Ethers

This reaction leads to processes similar to those which take place in the interaction of these ethers with diethylaniline, as considered above. However, this reaction takes place much more smoothly, i.e., its ionic character is still more strongly expressed.

5. The Action of Metallic Sodium

The reaction of α-bromoethyl alkyl ethers with sodium also confirms the ionic character of the α-bromine, seeing that if the bromine formed a covalent bond with the α-carbon, this would enable us to carry out the Wurtz synthesis. However, in this case we obtain results similar to those obtained by the action of organic and inorganic bases on the α-bromo ethers. In addition to acetals, these reactions give small amounts of butyl alcohol, whose formation is possible from the decomposition of the α-bromo ether. The mechanism of this reaction may be indicated in the following manner:

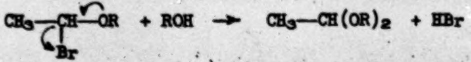
a)



$$CH_3—\underset{Br}{CH}—OR + Na \rightarrow NaBr + [CH_3—CH—OR]^+ + e$$

b) $[CH_3—CH—OR]^+ + e \longrightarrow [CH_3—CH—OR]$

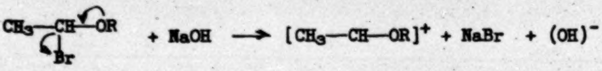
c) $[CH_3—\underset{|}{CH}—OR] \longrightarrow ROH + CH{\equiv}CH + H^+$

d) 

$$CH_3-\underset{Br}{CH}-OR + ROH \rightarrow CH_3-CH(OR)_2 + HBr$$

6. The Reaction of α-Bromomethyl Alkyl Ethers with Alcoholic Solutions of KOH

This reaction is accompanied by the formation of the $[CH_3-CH-OR]$ ion, followed by the addition of a second alkoxy, and subsequent formation of the corresponding acetal, in accordance with the following mechanism:

a) 

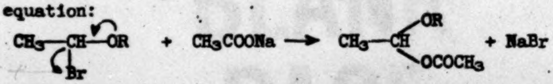
$$CH_3-\underset{Br}{CH}-OR + NaOH \rightarrow [CH_3-CH-OR]^+ + NaBr + (OH)^-$$

b) $[CH_3-CH-OR]^+ + ROH + (OH)^- \rightarrow CH_3-CH(OR)_2 + H_2O.$

7. The Reaction of α-Bromoethyl Alkyl Ethers with Acetic Acid and Sodium Acetate

Attempts to add acetic acid to α-bromoethyl alkyl ethers did not result in the formation of alkoxyethylidene acetates, although their formation might have been predicted on the basis of the decomposition products which were isolated (alcohol, and a dark tarry residue). We further investigated the reaction of α-bromoethyl alkyl ethers with fused sodium acetate in solvents.

This reaction led to the synthesis of alkoxyethylidene acetates according to the following equation:



$$CH_3-\underset{Br}{CH}-OR + CH_3COONa \rightarrow CH_3-CH\begin{matrix}OR\\OCOCH_3\end{matrix} + NaBr$$

It also showed the great stability of the lower members of the homologous series of α-bromo ethers in comparison with the higher. Thus, under the same conditions, α-bromodiethyl ether in petroleum ether medium gave ethoxyethylidene acetate in a yield 63% of the theoretical, and in dioxane medium, it gave 87% of the theoretical. α-Bromoethyl butyl alcohol in petroleum ether medium did not give the acetal-acylal, but decomposed to give butyl alcohol, and in dioxane medium gave only 45% of the theoretical yield.

8. The Reaction of Hydrogen Chloride with α-Bromoethyl Alkyl Ethers

It is known [1] that in the α-chloroethyl alkyl ethers, the chlorine is easily replaced by bromine under the action of hydrogen bromide. In the present work we showed that the reverse replacement of bromine by chlorine under the action of hydrogen chloride on the α-bromoalkyl ethers did not take place.

α-Bromoethyl alkyl ethers are colorless, transparent liquids which fume in the air. As a result of the extreme instability of these compounds, they are very sensitive to the action of water, light, and heat [5].

With an increase in the molecular weight of the radical, their stability decreases. Thus, α-bromoethyl methyl ether is the most stable of the entire homologous series of these compounds. It distills under normal pressure with only slight decomposition, and may be stored fof 8 days in a flask with a ground-in stopper without appreciable decomposition, while the other α-bromoethyl alkyl ethers can not be stored for more than 1 or 2 days. α-Bromoethyl alkyl ethers are very effective reagents for producing polymerization in vinyl ethers.

EXPERIMENTAL

I. The Synthesis of α-Bromoethyl Alkyl Ethers

For the synthesis of the α-bromoethyl alkyl ethers, we used the vinyl alkyl ethers, obtained by the method of Favorsky and Shostakovsky [6], and purified by the method used in the Laboratory of Vinyl Compounds.

1. The Synthesis of α-Bromoethyl Butyl Ether.

100 g of vinyl butyl ether, with the following characteristics: b.p. 93-95°; n_D^{20} 1.4020; d_4^{20} 0.7788, was placed in a flask fitted with a stirrer, a reflux condenser, a thermometer, and a tube for the passage of hydrogen bromide. The reaction flask was placed in a cooling mixture, and the temperature in the flask maintained about zero. Using energetic stirring, the hydrogen bromide was passed in at a moderate rate, the latter being regulated by the temperature in the flask. The hydrogen bromide was obtained by the addition of bromine drop by drop to a mixture of red phosphorus and water, with stirring. Then the hydrogen bromide was passed through a column containing glass wool impregnated with moist red phosphorus, and through two more tubes containing calcium chloride. The latter were immersed in a cooling mixture to cool the hydrogen bromide. After the hydrogen bromide had been passed in for eight hours, it began to come through the opening of a calcium chloride tube which was placed at the end of the reflux condenser. This indicated that the vinyl butyl ether was saturated with hydrogen bromide, and that the reaction was complete. Weighing of the reaction flask showed that the reaction mixture had gained 82.5 g in weight.

A vacuum fractionation gave 160.8 g of α-bromoethyl n-butyl ether. The α-bromo ether we obtained was a transparent colorless liquid which fused in the air. Its yield was 88.9% of the theoretical. The characteristics of α-bromoethyl n-butyl ether are:

B.p. 57-58° (10 mm); n_D^{20} 1.4485; d_4^{20} 1.2086; MR_D 40.08.
$C_6H_{13}OBr$. Computed: MR_D 39.31.

Determination of molecular weight:

0.1200 g substance: 15.1 g benzene: Δt 0.23°.
0.2611 g substance: 15.1 g benzene: Δt 0.50°.
Found: M 176.9, 177.1
$C_6H_{13}OBr$. Computed: M 180.9.

Elementary analysis:

5.38 mg substance: 8.00 mg CO_2; 3.61 mg H_2O.
5.26 mg substance: 7.81 mg CO_2; 3.51 mg H_2O.
Found %: C 40.55, 40.49; H 7.51, 7.47.
$C_6H_{13}OBr$. Computed %: C 39.80; H 7.18.

Determination of bromine (Volhard):

0.1664 g substance: 20.0 ml 0.1 $AgNO_3$; 10.96 ml 0.1 NH_4CNS.
0.1853 g substance: 20.0 ml 0.1 $AgNO_3$; 10.88 ml 0.1 NH_4CNS.
Found %: Br 43.42, 43.65.
$C_6H_{13}OBr$. Computed %: Br 44.17.

2. The Synthesis of α-Bromodiethyl Ether

52 g of vinyl ether was used, with the following characteristics: b.p. 35.5-36°; n_D^{20} 1.3785; d_4^{20} 0.7542; saturation with hydrogen bromide took place in 6 hours. The gain in weight was 71 g. 92 g of α-bromodiethyl ether was obtained, boiling at 40-41° at 42 mm, with the following characteristics:

n_D^{20} 1.4465; d_4^{20} 1.2770; MR_D 31.94.
C_4H_9OBr. Computed: MR_D 30.08.

The yield of α-bromodiethyl ether was 84% of the theoretical.

Determination of molecular weight:

0.1301 g substance: 14.5 g benzene: Δt 0.310°.
0.2510 g substance: 14.5 g benzene: Δt 0.595°.
Found: M 148.2, 149.0.
C_4H_9OBr. Computed: M 152.9.

Elementary analysis:

6.20 mg substance: 7.21 mg CO_2; 6.35 mg H_2O.
6.02 mg substance: 6.99 mg CO_2; 6.30 mg H_2O.
Found %: C 31.77, 31.67; H 5.74, 5.86.
C_4H_9OBr. Computed %: C 31.40; H 5.89.

Determination of bromine (Volhard):

0.3200 g substance: 25.0 ml 0.1 N $AgNO_3$; 4.42 ml 0.1 N NH_4CNS
0.3108 g substance: 25.0 ml 0.1 N $AgNO_3$; 4.65 ml 0.1 N NH_4CNS
Found %: Br 51.40, 52.33.
C_4H_9OBr. Computed %: Br 52.26.

The specific gravity which we found for α-bromodiethyl ether did not coincide with that found by Henry [2], who distilled α-bromodiethyl ether at normal pressure. This, apparently, was the cause of his low result..

3. The Synthesis of α-Bromoethyl Methyl Ether

37.5 g of vinyl methyl ether was used, with the following characteristics:

B.p. 5-5.2° at 745 mm; n_D^0 1.3730; d_4^0 0.7723 [7].

Saturation with hydrogen bromide took place in 6 hours. Gain in weight, 44 g.

The α-bromoethyl methyl ether obtained was in the amount of 75.5 g. It boiled at 56.5-57° (158 mm), and had the following characteristics:

n_D^{20} 1.4486; d_4^{20} 1.4253; MR_D 26.11.
C_3H_7OBr. Computed: MR_D 25.46.

The yield of α-bromoethyl methyl ether was 85% of theory.

Determination of molecular weight:

0.2010 g substance: 15.0 g benzene: Δt 0.52°.
0.4102 g substance: 15.0 g benzene: Δt 0.104°.
Found: M 132.0, 134.6.
C_3H_7OBr. Computed: M 138.9.

Determination of bromine (Volhard):

0.1360 g substance: 24.51 ml 0.1 N $AgNO_3$; 14.74 ml NH_4CNS
0.1566 g substance: 24.51 ml 0.1 N $AgNO_3$; 13.25 ml NH_4CNS
Found %: Br 57.06, 57.16.
C_3H_7OBr. Computed %: Br 57.54.

II. The Investigation of the Properties of α-Bromoethyl Alkyl Ethers

Below we give an example of each reaction of a number of experiments carried out with α-bromoethyl methyl, α-bromoethyl ethyl, and α-bromoethyl n-butyl ethers.

1. The Titration of α-Bromoethyl Alkyl Ethers with 0.1 N NaOH

Samples of freshly distilled α-bromo ethers were titrated with 0.1 N NaOH in the presence of methyl orange as indicator.

For 0.1379 g of α-bromoethyl methyl ether, 9.55 ml of 0.1 N NaOH were required. This amounted to 98.50% of the H ion titrated.

For 0.3208 g of α-bromodiethyl ether, 19.8 ml of 0.1 N NaOH were required; this amounted to 98.06% of the H ion titrated.

For 0.1467 g of α-bromoethyl n-butyl ether, 7.90 ml of 0.1 N NaOH were required; this amounted to 98.87% of the H ion titrated.

For calculation, we used the formula:

$$\% \text{ H} = \frac{0.004 \cdot M \cdot 100 \text{ ml } 0.1 \text{ N NaOH}}{40 \cdot \text{ weighed portion}}$$

where M is the molecular weight of the ether titrated.

2. The Determination of Bromine by Volhard's Method

In a flask with a ground-in stopper, containing 25 ml of distilled water and 20 ml of 0.1 N $AgNO_3$, we placed an ampoule containing a sample of the α-bromoether. The ampoule was shattered, the solution shaken well, and the excess of $AgNO_3$ titrated with 0.1 N NH_4CNS. The results of the titration of the α-bromo ethers by the Volhard method are listed with the analytical data giving the characteristics of each ether.

3. The Hydrolysis and Determination of Acetaldehyde in α-Bromoethyl Alkyl Ethers

The hydrolysis of the α-bromo ethers was carried out by the bisulfite method, used in the Laboratory of Vinyl Compounds. In a flask with a ground-in stopper we placed 20 ml of a fresh solution of bisulfite and to this we added the sample of α-bromo ether. After 15 minutes of shaking, followed by allowing the solution to stand for the same time, the bisulfite was titrated with a 0.1 N solution of iodine.

0.1210 g of α-bromoethyl n-butyl ether and 20 ml of bisulfite were used.

The back titration required 7.3 ml of 0.1 N I_2, which corresponded to 98.0% of the acetaldehyde theoretically possible.

0.1198 g of α-bromoethyl n-butyl ether and 20 ml of bisulfite were used. The back titration required 7.9 ml of 0.1 N I_2, which corresponded to 98.60% of the acetaldehyde theoretically possible.

20.0 ml of the bisulfite solution used up 20.4 ml of 0.1 N I_2. The calculation was carried out by means of the formula:

$$\% \text{ CH}_3\text{CHO} = \frac{0.17348 \cdot 0.01269 \cdot M(b - c)}{a}$$

where 0.17348 is Ripper's constant [7],

a is the sample of α-bromo ether, in grams,

b is the number of ml of 0.1 N I_2 used up in titrating the bisulfite,

c is the number of ml of 0.1 N I_2 used up in titrating the excess of bisulfite,

M is the molecular weight of the α-bromo ether.

4. The Reaction of α-Bromoethyl Alkyl Ethers with Diphenylaniline

In a flask fitted with a stirrer, a reflux condenser, a thermometer, and a dripping funnel, 26 g of α-bromoethyl n-butyl ether was added drop by drop over a period of 2 hours to 21.4 g of diethylaniline. The temperature of the reaction mixture was maintained about +5°. At the end of the reaction, 32.5 g of diethylaniline hydrobromide were filtered off. The liquid phase gave 11.2 g of a product which boiled at 185-186°, and had the following characteristics:

n_D^{20} 1.4080; d_4^{20} 0.8280; MR_D 51.84.
$C_{10}H_{22}O_2$. Computed: MR_D 51.67.

Determination of molecular weight:

0.1168 g substance: 13.6 g benzene: Δt 0.28°.
0.2280 g substance: 13.6 g benzene: Δt 0.50°.
Found: M 165.7, 171.7.
$C_{10}H_{22}O_2$. Computed: M 174.0.

The product obtained was dibutyl acetal. The yield was 90% of theory.

The constants obtained for dibutyl acetal were close to those given in the literature [2,8]. The same product was obtained when double the amount of diethylaniline was used, or when the reaction was carried out in the presence of of butyl alcohol. In these cases, the yield of dibutyl acetal amounted to 88% of theory.

5. The Reaction of α-Bromoethyl Alkyl Ethers with Ammonia

Dry ammonia was passed into a three-necked flask which was fitted with a reflux condenser, and a thermometer and contained 40 g of α-bromoethyl n-butyl ether in 20 g of ethyl ether. During this, the temperature rose to 42°. Treatment of the product obtained gave 30 g of ammonium bromide, contaminated with tar, 14 g of dibutyl acetal with b.p. 185-186°, n_D^{20} 1.4060, d_4^{20} 0.8278· 4.0 g of butyl alcohol, b.p. 116.5-117°; n_D^{20}1.4000, d_4^{20} 0.8088, and a small polymerized residue.

The yield of acetal amounted to 74% of theory.

6. The Reaction of α-Bromoethyl Alkyl Ethers with Metallic Sodium

9.0 g of α-bromoethyl n-butyl ether was added drop by drop, with stirring to 1.1 g of metallic sodium in ethyl ether in a three-necked flask. During this, the temperature rose to 42°. After 2 hours of heating on an oil bath up to 80°, the product was treated in the usual way to give 5 g of crystalline sodium bromide and 4 g of dibutyl acetal with b.p. 186-187°, n_D^{20} 1.4085, d_4^{20} 0.8288. A small amount of a fraction with b.p. 91-92°, n_D^{20}1.3970 and d_4^{20} 0.8524 was also obtained. Because of the small amount of the latter, it was impossible to decide whether this product was vinyl butyl ether, or a product of the partial reduction of the latter to give ethyl butyl ether.

7. The Reaction of α-Bromoethyl Alkyl Ethers with Alcoholic Alkali

a) The reaction of α-bromodiethyl ether with an alcoholic solution of caustic soda. 18 g of α-bromodiethyl ether were added to a saturated solution of an equimolecular amount of caustic soda in ethyl alcohol, contained in a flask fitted with a reflux condenser, a thermometer and a stirrer. The reaction temperature did not exceed 48°. After the entire quantity of the α-bromo ether had been added, the reaction mixture was heated up to 70° for 1 hour. The usual treatment gave 11.9 g of crystalline sodium bromide and 5 g of a fraction boiling at 102.5-103°, with the following characteristics:

n_D^{20} 1.3810; d_4^{20} 0.8301; MR_D 33.00.

$C_6H_{14}O_2$. Computed: MR_D 33.19

Determination of molecular weight:

0.1604 g substance: 13.44 g benzene; Δt 0.55°.
0.2810 g substance: 13.44 g benzene; Δt 0.92°.
Found: M 111.1, 116.4.
$C_6H_{14}O_2$. Computed: M 118.0.

The product obtained was diethyl acetal. Its characteristics were close to those obtained by other authors [9].

b) The reaction of α-bromoethyl methyl ether with an alcoholic solution of caustic soda. Under the same conditions as in the preceding experiment 26 g of α-bromoethyl methyl ether and 7.2 g of caustic soda in 50 ml of methyl alcohol gave 13.5 g of crystalline sodium bromide and 11.0 g of a fraction with b.p. 61-64°, from which dimethyl acetal was isolated with the following characteristics:

B.p. 63.5-64°; n_D^{20} 1.3760; d_4^{20} 0.8578.

These constants agree with the data of other authors [10]. The closeness of the boiling points of methyl alcohol (65°) and of dimethyl acetal (63.5-64°) makes it difficult to separate the latter in good yield.

8. The Reaction of α-Bromoethyl Alkyl Ethers with Sodium Acetate.

a) The reaction of α-bromodiethyl ether with sodium acetate in a solution of petroleum ether. 18.8 g of α-bromodiethyl ether in a solution of 24.5 g of petroleum ether (boiling range 40 to 60°) was added drop by drop to 11 g of powdered, fused sodium acetate at a temperature of +5 to +8°, with good stirring. The mixture was then heated to 50° for 2 hours and allowed to stand overnight. Filtration gave 14 g of crystalline sodium bromide and sodium acetate. After the petroleum ether had been driven off from the liquid product, it was fractinnated in vacuum three times. It gave 10.1 g of a fraction with b.p. 58-59° (38 mm), and the following characteristics:

n_D^{20} 1.3926; d_4^{20} 0.9458; MR_D 33.31.
$C_6H_{12}O_3$. Computed: MR_D 33.20.

The product obtained was ethoxyethylidene acetate. Its yield was 63% of theory. The constants found are close to those in the literature [1].

b) The reaction of α-bromodiethyl ether with sodium acetate in dioxane solution. Under similar conditions 18.5 g of α-bromodiethyl ether 25 g of absolute dioxane, and 10.5 g of sodium acetate were used for the reaction. Filtration gave 14 g of crystalline sodium bromide and sodium acetate. The dioxane was driven off from the liquid product and the latter distilled in vacuum three times.

14.1 g of the fraction boiling at 48-50° at 41 mm was obtained. It had the following characteristics:

n_D^{20} 1.3930; d_4^{20} 0.9442; MR_D 33.37.
$C_6H_{12}O_3$. Computed MR_D 33.20.

The product obtained was ethoxyethylidene acetate. The yield was 87% of theory. The constants obtained were close to those in the literature [1].

c) The reaction of α-bromoethyl butyl ether and sodium acetate in a solution of petroleum ether. Under the same conditions, 25 g of sodium acetate and 15 g α-bromoethyl n-butyl ether in 28 g of petroleum ether gave 3.8 g of a product which had the following characteristics:

B.p. 117-118°; n_D^{20} 1.4000; d_4^{20} 0.8088; MR_D 22.20.
$C_4H_{10}O$. Computed: MR_D 22.19.

The product obtained was butyl alcohol. In this experiment, its yield was 62% of theory. Traces of acetic acid were found.

d) The reaction of α-bromoethyl n-butyl ether with sodium acetate in a solution of dioxane. Under the same conditions 14 g of α-bromoethyl n-butyl ether and 8 g of sodium acetate in 20 g of absolute dioxane gave 7.8 g of a crystalline precipitate of sodium bromide and sodium acetate. After three distillations in vacuum, the liquid product gave 6.8 g of a fraction with the following characteristics:

B.p. 66-67°(10 mm); n_D^{20} 1.4030; d_4^{20} 0.9187; MR_D 42.56.
$C_8H_{16}O_3$. Computed : MR_D 42.44.

This product was butoxyethylidene acetate. The constants obtained are close to those given in the literature [11]. The yield of butoxyethylidene acetate was 45% of theory.

9. The Reaction of α-Bromodiethyl Ether with Hydrogen Chloride.

In a flask fitted with a reflux condenser, a thermometer, and a stirrer, there was placed 31.5 g of freshly distilled α-bromodiethyl ether with b.p. 40-41° at 42 mm. Through the α-bromo ether, dry hydrogen chloride was passed at room temperature for a period of 3.5 hours. During this, the temperature did not rise, and the appearance of the compound did not change. Upon distillation in vacuum, the compound distilled over almost completely within the limits from 31 to 32° (at 28 mm) (30 g distilled over). It had the following characteristics:

n_D^{20} 1.4400; d_4^{20} 1.2770; MR_D 31.57; C_4H_9OBr. Computed: MR_D 30.08.

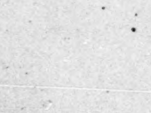
0.1601 g substance: 24.51 ml 0.1 N $AgNO_3$; 14.21 ml 0.1 N NH_4CNS
0.1903 g substance: 24.51 ml 0.1 N $AgNO_3$; 12.18 ml 0.1 N NH_4CNS.
Found %: Br 51.42, 51.78.
C_4H_9OBr. Computed %: Br 52.26.

SUMMARY

1. α-Bromoethyl methyl, α-bromodiethyl, and α-bromoethyl n-butyl ethers have been synthesized from the corresponding vinyl alkyl ethers. Their structure and properties have been determined by means of their reactions with various reagents. The probable mechanisms of these reactions have been given.

2. It has been found that the splitting off of hydrogen bromide by the action of inorganic and organic bases on α-bromoethyl alkyl ethers to give the corresponding vinyl alkyl ethers is impossible.

3. It has been shown that the α-bromoethyl alkyl ethers are very reactive in comparison with the corresponding α-chloro ethers. This reactivity is connected with the peculiarities of structure of these compounds, and we may assume the existence of mesomeric effects such as the following in their molecules.



It follows from this that the α-bromine is attached to the carbon by an almost ionic bond.

LITERATURE CITED

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* See CB translatiol p. 1379 ff.

INVESTIGATIONS IN THE DOMAIN OF THE SYNTHESIS AND TRANSFORMATIONS OF α-HALOGEN ETHERS

III. α-HALOGEN-ETHYL PHENYL ETHERS

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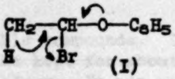
The present investigation is directly related to the study of the α-halogen-ethyl alkyl ethers [1,2]. α-Halogen-ethyl phenyl ethers are not described in the literature, and only a single patent [3] describes the preparation of α-chloroethyl phenyl ether.

The synthesis of α-halogen-ethyl phenyl ethers was carried out by us under the same conditions as that of α-halogen-ethyl alkyl ethers, according to the following equation: $CH_2{=}CH{-}OC_6H_5 + H.Hal \longrightarrow CH_3{-}CHHal{-}OC_6H_5$.

From a study of the α-halogen ethyl phenyl ethers, we arrived at the conclusion that their properties were in accord with the generally accepted ideas about the structure of this group of compounds, i.e., that the formula $CH_3{-}CHHal{-}OC_6H_5$ (I) gives the best picture of the true situation in their molecules, while at the same time permitting the existence of mesomeric effects.

The mesomeric effect in the side chain:

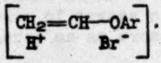


(I)

makes it possible to express the condition of the molecule by the following mesomeric structures:

$$[CH_3{-}CH{=}O^{+}{-}Ar]Br^{-}\ ;\qquad [CH_3{-}\overset{+}{C}H{-}OAr]Br^{-};$$

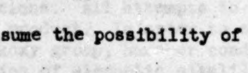
(II) (III)



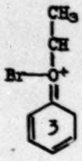
$$\begin{bmatrix} CH_2{=}CH{-}OAr \\ H^{+} \quad\quad Br^{-} \end{bmatrix}.$$

(IV)

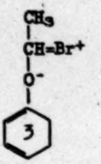
The presence of a benzene nucleus in these compounds makes it possible for the following mesomeric effects to appear, in opposition to the direction of the preceding effects:



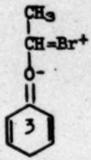
from this effect we can assume the possibility of such structures as:



(V)

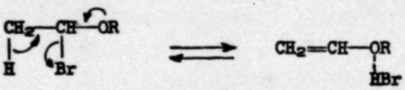


(VI)



(VII)

Because of the presence of the mesomeric effects in opposing directinns, as described above, within the α-halogen-ethyl phenyl ether molecules, these ethers show very complicated combinations of different tendencies. Still, it is possible to assert that of the total number of possible structures, the dominant role belongs to those structures in which the α-halogen forms an almost covalent bond. Because of this, we must not expect that the α-halogen phenyl ethers will show the presence of tautomerism, as is present in α-halogen alkyl ethers:



The absence of such tautomerism is confirmed by the chemical behavior of α-halogen phenyl ethers. The predominance of the structure in which the α-halogen is close to a covalent condition in the α-halogen-ethyl phenyl ethers is the chief reason for the differences in the properties between the α-halogen phenyl and alkyl ethers. This difference is expecially clearly evident in the examples of chemical behavior of the α-halogen-ethyl phenyl ethers.

In contrast to the α-halogen alkyl ethers, α-halogen phenyl ethers:

1) do not have their chlorine substituted by bromine when bromine or hydrogen bromide act upon α-chloroethyl phenyl ethers;

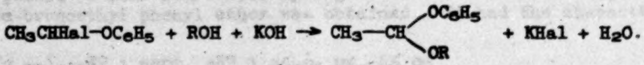
2) do not give phenoxyethylidene acetates by the action of acetic acid and the latter's salts;

3) are considerably more stable compounds. In an atmosphere of dry air, α-halogen-ethyl phenyl ethers may be kept for about 8 days, while α-halogen alkyl ethers can be kept only one or two days. In air, α-halogen phenyl ethers give off hydrogen halide, with the formation of polymeric products. In this case, traces of moisture in the air have a catalytic influence, and not the oxygen. This is confirmed by carrying out the reactions of these ethers in an inert medium. Here we observe an analogy with the catalytic influence of traces of hydrogen halide acids in the transformations of vinyl-alkyl ethers, as an excess of these acids leads to an addition reaction.

There are also well characterized differences between α-halogen alkyl and phenyl ethers in the reactions with diethylaniline and with alcohols.

The reaction of α-halogen phenyl ethers with diethylaniline is accompanied by the formation of only small amounts of vinyl phenyl ether. At the same time, phenol and diphenyl acetal are also formed.

The reaction of α-halogen phenyl ethers with alcohols does not, in general, take place under the usual conditions. All attempts to cause addition inevitably led to the polymerization of the product. In order to substitute the halogen in α-halogen phenyl ethers by an alkoxy group, harsher conditions are required (the presence of a concentrated solution of alcoholic alkali). The reaction then took place according to the following equation:



$$CH_3CHHal\text{-}OC_6H_5 + ROH + KOH \rightarrow CH_3\text{—}CH\begin{smallmatrix}OC_6H_5\\ OR\end{smallmatrix} + KHal + H_2O.$$

A property common to the α-halogen alkyl and phenyl ethers is their tendency to undergo hydrolytic cleavage. However, in this case too, some difference is to be observed in the velocity of this reaction. It takes place more slowly with α-halogen phenyl ethers. Hydrolysis proceeds according to the following equation:

$$CH_3\text{-}CHHal\text{-}OC_6H_5 + H_2O \longrightarrow CH_3CHO + C_6H_5OH + HHal.$$

The hydrogen halide which is formed may be titrated with 0.1 N alkali, or determined by means of its halogen content, by Volhard's method.

α-Halogen phenyl ethers, like α-halogen alkyl ethers, are excellent catalytic agents for the polymerization of vinyl-alkyl ethers.

EXPERIMENTAL

I. The Synthesis of α-Halogen-ethyl Phenyl Ethers

Vinyl phenyl ether, obtained by the method of Favòrsky and Shostakovsky [4], and purified by the method used in the Laboratory of Vinyl Compounds [1], was placed in a three-necked flask which was fitted with a thermometer, stirrer, and a reflux condenser to which a calcium chloride tube was attached. The ether had the following constants:

B.p. 155-156°; n_D^{20} 1.5225; d_4^{20} 0.9767.

With good stirring, and cooling below zero, a moderate current of dry hydrogen halide was passed through, its velocity being regulated by the temperature inside the flask. The reaction was continued until the system was completely saturated with hydrogen halide.

1. The synthesis of α-chloroethyl phenyl ether. 33 g of vinyl phenyl ether were saturated over a period of 3 hours with hydrogen chloride. Gain in weight 10 g. 41 g of α-chloroethyl phenyl ether was obtained. It had the following characteristics:

B.p. 97-98° (24 mm); n_D^{20} 1.5225; d_4^{20} 1.1150; MR_D 42.80.

C_8H_9OCl 3F. Computed: MR_D 42.05.

The yield of α-chloroethyl phenyl ether was 95.5% of theory.

Determination of molecular weight:

0.1402 g substance: 15.8 g benzene: Δt 0.03°.
0.2553 g substance: 15.8 g benzene: Δt 0.055°
Found: M 151.44, 151.42.
C_8H_9OCl. Computed: M 156.5.

Elementary analysis:

4.280 mg substance: 9.597 mg CO_2; 2.245 mg H_2O.
3.945 mg substance: 8.820 mg CO_2; 2.124 mg H_2O.
Found %: C 61.18, 61.49; H 5.82, 5.94.
C_8H_9OCl. Computed %: C 61.34; H 5.75.
6.810 mg substance: 6.175 mg AgCl.
6.770 mg substance: 6.207 mg AgCl.
Found %: Cl 22.43, 22.68.
C_8H_9OCl. Computed %: Cl 22.68.

2. The synthesis of α-bromoethyl phenyl ether. 35.9 g of vinyl phenyl ether was saturated in a period of four hours with hydrogen bromide. Gain in weight 23.4 g. 50.5 g of α-bromoethyl phenyl ether was obtained. It had the characteristics:

B.p. 87-89° (7 mm); n_D^{20} 1.5500; d_4^{20} 1.3640; MR_D 46.96.

C_8H_9OBr Γ_3. Computed: MR_D 44.95.

The yield of α-bromoethyl phenyl ether was 95.4% of theory.

Determination of molecular weight:

0.1880 g substance: 16.2 g benzene: Δt 0.03°.
0.3801 g substance: 16.2 g benzene: Δt 0.06°.
Found: M 198.06, 200.20.
C_8H_9OBr. Computed : M 200.9.

Determination of bromine (Volhard):

0.1400 g substance: 20.0 ml 0.1 N $AgNO_3$; 13.10 ml 0.1 N NH_4CNS
0.1532 g substance: 20.0 ml 0.1 N $AgNO_3$; 12.40 ml 0.1 N NH_4CNS.
Found %: Br 39.38, 39.64.
C_8H_9OBr. Computed %: Br 39.77.

II. The Transformations of α-Halogen-ethyl Phenyl Ethers

1. The hydrolysis of α-chloroethyl phenyl ether. A sample of α-chloroethyl phenyl ether, in an ampoule, was placed in an Erlenmeyer flask with a ground glass stopper which contained 20 ml of distilled water and 40 ml of a 0.2 N solution of bisulfite. The ampoule was broken and the solution stirred for 45 minutes. The excess of bisulfite was then titrated with 0.1 N iodine solution.

0.1658 g substance: 40 ml 0.2 N bisulfite; 3.7 ml 0.1 N I_2.
0.1726 g substance: 40 ml 0.2 N bisulfite; 3.9 ml 0.1 N I_2.
for 40 ml 0.2 N bisulfite; 25.2 ml 0.1 N I_2 used.
Found %: CH_3CHO 99.50, 99.86 of theory.

For the details of the method, cf. [2].

2. The titration of α-chloroethyl phenyl ether with a 0.1 N solution of NaOH. A sample of α-chloroethyl phenyl ether, in an ampoule, was placed in a flask with a ground-glass stopper containing 25 ml of distilled water, then broken, and titrated with 0.1 N NaOH in the presence of methyl orange.

0.2750 g substance: 16.5 ml 0.1 N NaOH.
0.2516 g substance: 15.2 ml 0.1 N NaOH.
Found %: H titrated 98.89, 99.58.

For the formula used in calculation, cf. [2].

3. The determination of chlorine in α-chloroethyl phenyl ether, by Volhard's method. The ampoule containing a sample of the α-chloroether was placed in a flask with a ground-glass stopper containing 0.1 N $AgNO_3$ solution, then broken, the solution stirred, and the excess of $AgNO_3$ titrated with 0.1 N solution of NH_4CNS.

0.1520 g substance: 20 ml 0.1 N $AgNO_3$; 8.4 ml 0.1 N NH_4CNS.
0.1493 g substance: 20 ml 0.1 N $AgNO_3$; 8.6 ml 0.1 N NH_4CNS.
Found %: Cl 22.46, 22.30.
C_8H_9OCl. Computed %: Cl 22.68.

4. The reaction of α-chloroethyl phenyl ether with alcohol and alcoholic alkali.

a) The reaction of α-chloroethyl phenyl ether with butyl alcohol under ordinary conditions. 20.6 g of α-chloroethyl phenyl ether was mixed with 8.8 g of butyl alcohol at room temperature, with vigorous stirring. Thirty minutes after the entire quantity of butyl alcohol had been added, the product polymerized into a red, transparent, viscous polymer.

b) The reaction of α-chloroethyl phenyl ether with butyl alcohol at low temperature and in an atmosphere of nitrogen. 15.6 g of α-chloroethyl phenyl ether was mixed with 21.0 g of butyl alcohol at -12° in an atmosphere produced by a slow stream of nitrogen. Twenty minutes after the addition of the butyl alcohol, the entire compound had been transformed into a viscous polymer with a red color. When this was fractionated in vacuum, it gave 15 g of butyl alcohol.

c) The reaction of α-chloroethyl phenyl ether with a solution of caustic potash in ethyl alcohol. 23.5 g of α-chloroethyl phenyl ether was added drop by drop, with stirring, to a solution of 8.5 g of caustic potash in 75 ml of ethyl alcohol. The temperature of the reaction mixture was kept between +5° and + 7°. On the following day, 10.5 g of crystalline potassium chloride was separated by filtration, and the liquid product was distilled to give ethyl alcohol, plus 20 g of a fraction with b.p. 134-137° (at 107 mm). The latter fraction was distilled twice in vacuum to give a product which had the following characteristics:

B.p. 70-71° (4 mm); $n_D^{21.5}$ 1.4930; $d_4^{21.5}$ 0.9932; MR_D 48.57.

$C_{10}H_{14}O_2 \Gamma_3$. Computed: MR_D 48.07.

The yield of ethylphenyl acetal was 88% of theory.

Elementary analysis:

4.526 mg substance: 11.961 mg CO_2; 3.350 mg H_2O.
4.650 mg substance: 12.338 mg CO_2; 3.522 mg H_2O.
Found %: C 72.12, 72.41; H 8.28, 8.47.
$C_{10}H_{14}O_2$. Computed %: C 72.30; H 8.43.

d) The reaction of α-chloroethyl phenyl ether with a solution of KOH in butyl alcohol. 25.6 g of α-chloroethyl phenyl ether was added drop by drop, with stirring and cooling, to a solution of 9.4 g of caustic potash in 80 ml of butyl alcohol. The temperature of the reaction mixture was kept within the limits of +5 to +10°. 11.8 g of crystalline potassium chloride were filtered off. The liquid product was distilled in vacuum to give 21.2 g of a fraction with b.p. 138-142° (at 38 mm). From this fraction, careful distillation in vacuum gave a product which had the following characteristics:

B.p. 125-127° (21 mm); n_D^{24} 1.4825; d_4^{24} 0.9595; MR_D 57.69.

$C_{12}H_{18}O_2\ 3\Gamma$. Computed: MR_D 57.30.

This product was butylphenyl acetal.

The constants obtained by us are close to those given in the literature [5].

5. The Reaction of α-Chloroethyl Phenyl Ether with Acetic Acid and Sodium Acetate.

a) The reaction of α-chloroethyl phenyl ether with acetic acid. To 13 g of glacial acetic acid, there was gradually added, at room temperature, 25.5 g of α-chloroethyl phenyl ether. The mixture was then heated to 85° for an hour; during the heating, the evolution of hydrogen chloride was observed, along with polymerization of the product to form a dark, very viscous polymer.

b) The reaction of α-chloro phenyl ether with sodium acetate. 39.0 g of the α-chloroethyl phenyl was added, with stirring, to a mixture of 30.0 g of fused sodium acetate in 40 ml of ethyl ether. After all the α-chloro ether had been added, the temperature of the reaction mixture was raised to 40°, and kept at that point for 2 hours. On the following day, 30 g of crystalline precipitate was filtered off. This contained no halogen (negative reaction by the test in Beilstein). The ethyl ether was distilled off from the liquid product, and the latter fractionated in vacuum to give 31 g of a substance which had the following characteristics:

B.p. 93-93.5° (17 mm); n_D^{22} 1.5210; d_4^{22} 1.1143.

This product was α-chloroethyl phenyl ether, recovered to the extent of 80% of the amount used for the reaction. The sodium acetate was recovered completely. No reaction took place.

6. The reaction of α-chloroethyl phenyl ether with bromine. To 24 g of α-chloroethyl phenyl ether at +4°, 3.5 g of bromine was added drop by drop. From the first drops on, the solution was colored red. A vacuum fractionation gave 21 g of α-chloroethyl phenyl ether with the following characteristics:

B.p. 98-100° (25 mm); n_D^{20} 1.5220; d_4^{20} 1.1152.

1 g of crystalline phenol and 1 g of tar were obtained. The same results were obtained when this reaction was attempted at +12°. The desired reaction did not take place.

7. The reaction of α-chloroethyl phenyl ether with hydrogen bromide. Hydrogen bromide was passed at +20° for 2 hours through a flask which contained 35 g of α-chloroethyl phenyl ether. Distillation in vacuum gave 31.8 g of α-chloroethyl phenyl ether, with the following characteristics:

B.p. 100-102° (30 mm); n_D^{20} 1.5215; d_4^{20} 1.1144.

The reaction did not take place. Of the α-chloro ether used, 91% was recovered.

8. The reaction of α-chloroethyl phenyl ether with diethylaniline. To 33.5 g of diethylaniline, 35.0 g of α-chloroethyl phenyl ether was added drop by drop while the temperature was raised to +35°. After all the α-chloro ether had been added, the product was allowed to stand until the following day. Filtration gave 38.2 g of crystalline diethylaniline hydrochloride, 18.5 g of a fraction with boiling range 116-145°, (at 28 mm), and 7.5 g of a fraction with boiling range 145-153° (at 28 mm). From these fractions, the following products were obtained: vinyl phenyl ether, which had the following characteristics:

B.p. 155-156°; n_D^{20} 1.5221; d_4^{20} 0.9773;

crystalline phenol, and diphenyl acetal, with the following characteristics:

B.p. 146-148° (37 mm); n_D^{20} 1.5540; d_4^{20} 1.0808.

SUMMARY

1. α-Chloro and α-bromoethyl phenyl ethers have been synthesized from vinyl phenyl ether. Their structure and properties have been determined by means of various transformations.

2. Differences have been found between the properties of α-halogen alkyl and α-halogen phenyl ethers. These include the lowered chemical reactivity of the latter, their greater stability toward storage, and their tendency, under the influences of traces of moisture, to form polymeric products.

3. The peculiarities in the behavior of α-halogen-ethyl phenyl ethers can be explained by the presence of the benzene nucleus in their molecule. In this connection, there arise not only the mesomeric effects, which characterize the α-halogen alkyl ethers, but a group of opposing mesomeric effects, which lower the ionic properties and increase the covalent properties of the α-halogen.

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